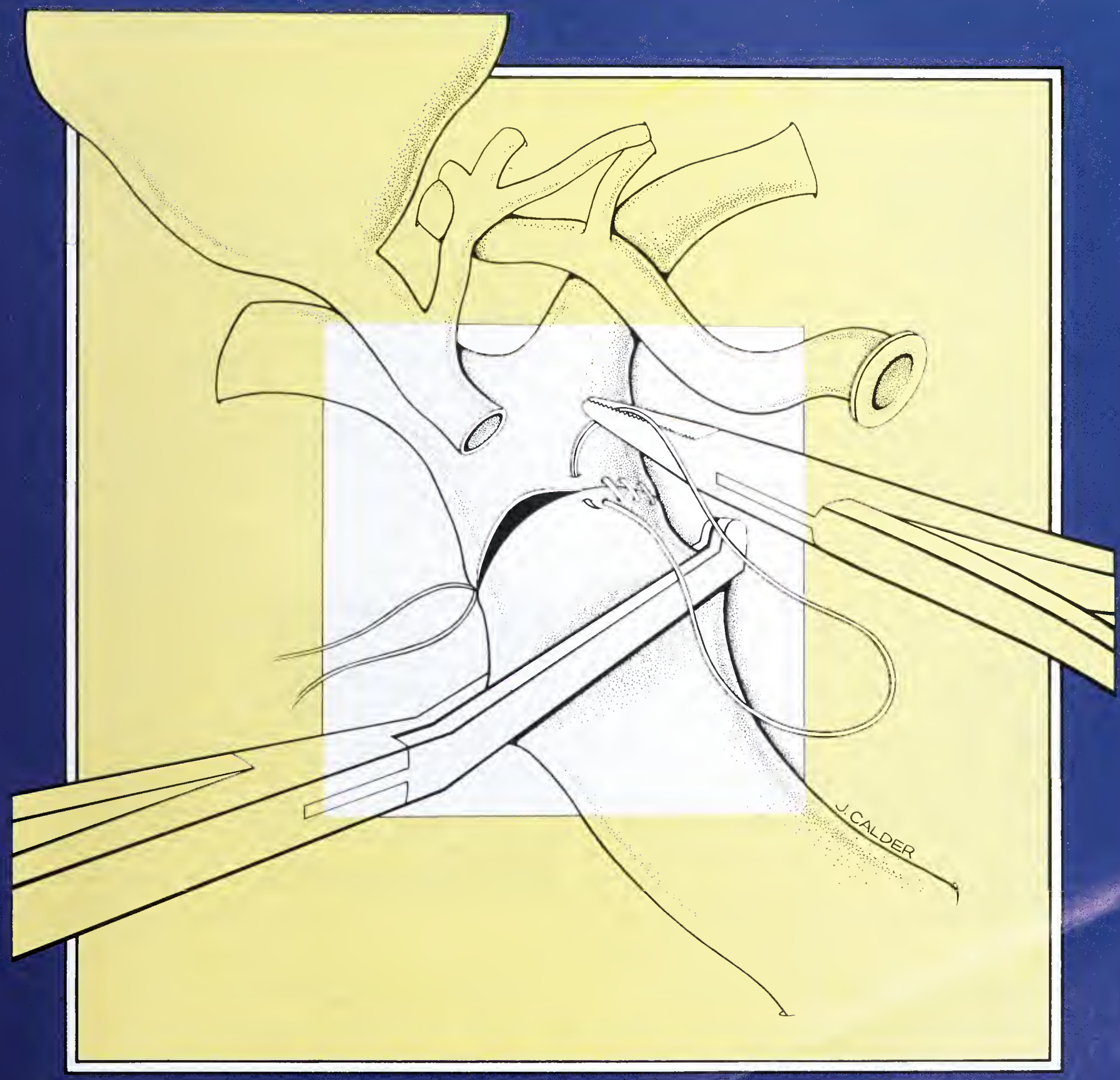
University of Toronto
MEDICAL JOURNAL
VOL LXIII NO. 2



FEATURE ARTICLES:
Liver Transplantation
A Severe Hand Injury

M D I C L® INC.

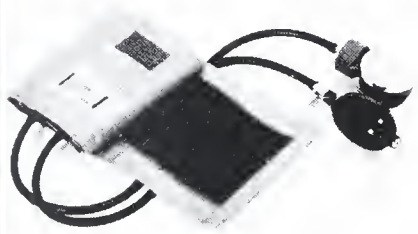
MDICL INC., introduces the latest in medical Electronics: ECG'S, ECG ANALYZERS, Monitors, Computerized Spirometers and much much more. Also a complete line of disposable and medical supplies at the most competitive prices.

MDICL INC.
175 TORYORK DRIVE, UNIT 6
WESTON, ONTARIO M9L 2Y7
TEL: 416-747-1125
TLX NBR: 06-23096 MDIC TOR

DEDICATED TO THE MEDICAL PROFESSION

SPECIAL FOR MEDICAL STUDENTS, DOCTORS ETC.

ANEROID SPHYGMOMANOMETER WITH POUCH



ONLY $9.99

DELUXE DUAL SIDED STETHOSCOPE

ONLY $5.99

DELUXE STAINLESS STEEL DUAL SIDED STETHOSCOPE

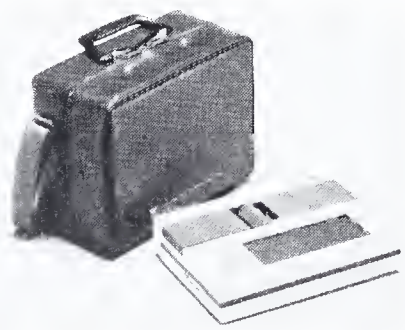
ONLY $14.99

SPRAGUE RAPPAPORT TYPE STETHOSCOPE

ONLY $15.99

THE HEART OF EVERY PRACTICE. MAKE IT YOURS.

FULLY AUTOMATIC PORTABLE ECG'S FROM FUKUDA M-E. MODEL CARDISUNY 501 A-B



WEIGHT: 1.5 Kg —
Size 24 × 17.5 × 4.8 cm.

Introducing the World's finest fully automatic, most compact and easy to use full 12-lead ECG. By the touch of a membrane key, it provides you in merely 45-seconds with a complete 12-lead trace. Ideal for use by: Doctors, Clinics, Hospital wards, Laboratories, Nursing Homes, house call or anywhere you require an ECG. A slick liquid crystal display keyboard contains all controls that are sealed to insure dust free & trouble free operation. Available in 3 ways: Dry cell, Dry cell adaptor combination, NICD Recharger, your choice. And the price is even more convincing.

FREE: LUXURIOUS CARRYING CASE FOR EASE OF STORAGE AND PORTABILITY

FULLY AUTOMATIC COMPUTERIZED SPIROMETERS FROM FUKUDA SANGYO

FUKUDA, the world's pioneers in the spirometry field for over 45 years, introduces a new generation of sophisticated spirometers: MODELS ST-100 and ST-200. Featuring the latest in micro-processor technology, instant LCD visual diaplay, instant graphic printout of all parameters & respiration waveforms. Its compact in design, portable and extremely simple to use. A carrying case is also available. A marvel of computer age technology. A classic HI-TECH...

Ideal for use in Hospital, Doctors offices, Clinics, Nursing Homes and Industries where high pollution is inherent.

COMPLETE YOUR PRACTICE WITH THESE MUST HAVE MODERN AGE EQUIPMENT.

COME VISIT OUR SHOWROOM. WE WILL ASSIST YOU IN SETTING-UP YOUR COMPLETE OFFICE WITH THE LATEST MEDICAL FURNITURE, EQUIPMENT & SUPPLIES. WE ARE YOUR ONE STOP MEDICAL SUPPLIER. WE WILL STRIVE TO ACHIEVE YOUR BEST POSSIBLE RESULTS. WE WILL DEFINITELY NOT EXTRA BILL YOU!

ALL OUR PRODUCTS CARRY A ONE YEAR WARRANTY. ORDERS OVER $300.00 ARE PREPAID. UNDER $300.00 PLEASE ADD $10.00 FOR SHIPPING & HANDLING. VISA & MASTER CHARGE ARE WELCOME. FINANCING AVAILABLE. VISA & MASTER CARD ARE ACCEPTED. CALL TODAY FOR YOUR ORDERS OR PLEASE WRITE US FOR FURTHER INFORMATION.

University of Toronto
MEDICAL JOURNAL
Established 1923. An Undergraduate Publication Volume 63, Number 2, March 1986

Editorial

We wish to welcome you to the second edition of the *Medical Journal*, 1985-1986. The theme of this issue focuses on the advancements in the various surgical specialities, as well as the psychosocial implications of surgery.

In this issue, we present a feature article on liver transplant by Riccardo A. Superina M.D. from Sick Children's Hospital. In this article, Dr. Superina summarizes the state of the art of liver transplantation with both a historical and current perspective.

John L. Semple M.D., a Senior Resident in Plastic Surgery at University of Toronto has also contributed an article on modern surgical management of the severely injured hand. He has taken the example of an ancient muzzle loading cannon injury and applied principles of modern plastic surgery to its management.

We hope you enjoy this issue. We wish to thank all our writers and staff for contributing to the production of this issue.

The Editors

Contents

Editorial 1

Liver Transplantation
Riccardo A. Superina 3

Severe Hand From Injury
John L. Semple 11

Tumour Arthroplasty
Richard W. McCalden 17

Immunogenic Cells within Bone Marrow
Karbi, Axelrod, Fernandes, Czitrom 23

The Separation of the Siamese Twin
M.E. Hoefert 26

Respirology Rounds — Question
Price, Hyland, Roscoe, Gray 31

The Spectrum Of Stroke
Mounsey, Parker, West, Whittle 32

Natural Progression From Life to Death
Blame Croll Papsin 37

The Psychological of
Mastectomy on Women
Pamela Stewart 40

Respirology Rounds — Answer
Price, Hyland, Roscoe, Gray 46

Patrons 48

Editorial Staff

Editors-in-chief:
Warren Mason, 8T7
Pamela Stewart, 8T7

Associate Editor:
Dan Poenaru, 8T6

Editorial Board:
Eva Chow, 8T7
Ed Etchells, 8T7
Lydia Hoh, 8T7
Mahmood Kara, 8T8
James Kim, 8T9
Susan Knabe, 8T7
Gabor Lantos, 8T7
Ann Li, 8T7
Robert Mounsey, 8T8
Anysia Rusak , 8T9
Michael Wong, 8T9

Medical Alumni Association

- **THE MEDICAL ALUMNI ASSOCIATION** is the bridge between the graduates and the Faculty of Medicine, University of Toronto.

- The Association provides financial assistance (scholarships, bursaries, travel grants, fellowships loans) for undergraduates, as well as sponsoring programs that are of particular interest — General Practice Panel, Arts and Letters Committee, Undergraduate Affairs, Graduation Banquet, etc.

- At the Faculty level, there are two representatives on the Faculty Council, a representative on the Admissions Committee, and the Chairman of the Student Aid Committee is a representative on the Student Awards Committee.

- At the University level, the Association has two representatives on the Universtiy of Toronto Alumni Association, two representatives on the College of Electors, and a representative on the Varsity Fund Executive Committee.

- We are also represented on various Search Committees when Department Chairmen and the Dean of Medicine are being sought.

- The Association is also involved in providing some impetus to five year reunions. Two letters will be sent free of charge, for each class celebrating their reunion. Every attempt is made to keep an up-to-date address list of all our graduates. Please remember to notify YOUR Medical Alumni Association of any address change.

- The Association is governed by graduates who give their time and talent voluntarily. There is one full time employee. Donations given for Student Aid are used entirely for that purpose. Trust funds are administered, without charge, following the direction of the donor.

Liver Transplantation

Riccardo A. Superina, M. D.

HISTORICAL

In the late 1950's and early 60's the early experimental work in orthotopic liver transplantation laid the groundwork for the first attempts in human liver transplantation by Thomas Starzl in Denver in 1963. Francis Moore in Boston and Starzl in Chicago both elaborated the procedures for harvesting and implanting livers in dogs in an orthotopic fashion after the removal of the recipient's own liver. These early animal experiments proved invaluable in highlighting the numerous technical problems of this operation, and provided opportunities for solving the problems of how to minimize cold and warm ischemia, how to divert portal blood flow during the anhepatic phase, and what the best methods of reconstructing the biliary outflow tract were. It also became apparent that auxiliary heterotopic liver allografts as described by Welch and Fortner were limited in their potential application primarily because of the mechanical difficulty of fitting a very large organ into a very limited space.

The first human transplants in Denver in 1963 were unsuccessful, and all the recipients died during, or soon after, the operation. Although the failures were due primarily to technical errors and difficulties, success seemed to be well within Starzl's grasp after his fourth recipient lived for twenty-two days only to die of sepsis. A moratorium lasting a few years was called. During this time it became clear that improved methods of immunosuppression were essential to prevent rejection, increase patient survival and decrease the devastating consequences of opportunistic infections.

The first trials of combination immunosuppression using both corticosteroids and azathioprine led to improved survival results in kidney transplant patients. The advent of anti-lymphocyte globulins (ALG) further improved the clinical ability to suppress rejection. These factors culminated in the resumption of the clinical liver transplant program in 1967 when a one and a half year old girl with unresectable hepatocellular carcinoma was given a new liver. This patient survived thirteen months only to succumb to recurrent cancer, but her relatively long-term survival represented the first truly successful liver transplant and signaled the beginning of extra-renal organ transplantation.

The following years brought mixed success. Survivors became more common occurrences but mortality, unfortunately, remained depressingly high at eighty percent. Surprisingly, perhaps, uncontrollable rejection was not a frequent cause of death; technical mistakes and mechanical problems, particularly troublesome with regard to the biliary anastomosis, accounted for the high mortality.

Over the sixteen year period 1963—1979, the Denver series grew to 170 patients. The one year survival rate remained steady at thirty-three percent, and twenty-six patients survived longer than five years. Most of the deaths occurred within three months of transplantation primarily because of poor recipient selection, technical problems including procurement injuries, and infection.

Calne in Cambridge and Pichlmayr in Hannover introduced liver transplantation to Europe after which major centres were established in the Netherlands and in Minnesota. These pioneer centres experimented and modified techniques and protocols, and served as training grounds for a future generation of liver transplant surgeons who have proliferated and have brought the operation home to an ever-expanding number of centres situated around the globe. Starzl's experience remains the largest, and in recent years following his move to the University of Pittsburgh, as the success rate and expectations from the operation have increased, the number of patients transplanted in Pittsburgh alone has increased to a stunning rate approaching three hundred per year. In Canada, the transplant team from the University of Western Ontario was the first to establish a strong liver transplant program, but more recently, successful transplants have also been carried out in Montreal and Halifax.

SOME NUMBERS

It has been estimated that ten to twenty liver transplants per million people per year are necessary to meet the requirements of patients dying of end-stage liver disease who would qualify as suitable candidates. In Canada, this translates into two to five hundred liver transplant patients per year and in the United States it has been estimated that there are three to four thousand potential liver transplant candidates yearly. Clearly, at the moment, the capacity to handle such large numbers does not exist.

Suitable transplant candidates range in age from early infancy to the middle fifties or, in exceptional circumstances, the early sixties. Historically, in Denver and Pittsburgh, forty to fifty percent of transplanted

THE CONCERNED PHYSICIAN

WHO WISHES TO SAVE ON DRUG COSTS FOR HIS PATIENTS SHOULD CONSIDER

novopharm

BRANDED GENERICS

novo-methacin Indomethacin
novo-naprox Naproxen
novo-pranol Propranolol HCl
novo-triamzide Triamterene-Hydrochlorothiazide

novopharm ltd.
1290 Ellesmere Road, Scarborough, Ontario, Canada M1P 2Y1
Telephone: (416) 291-8876

PAAB
CCPP

THE LARGEST CANADIAN OWNED COMPANY SPECIALIZING IN BRANDED GENERIC PHARMACEUTICAL PRODUCTS

patients have been children. During the years 1979 - 1982, over two hundred children died in Canada of biliary atresia and metabolic liver diseases alone.

Approximately three hundred would-be recipients are currently awaiting liver transplantation across North America in thirty medical centres. Although the shortage of organ donors has frequently been cited as the chief limiting factor determining the number of patients to be transplanted, a maldistribution of potential recipients among the different programs is also responsible for a certain degree of organ wastage.

Only twenty percent of liver donors referred to the Pittsburgh program during a recent period of time yielded organs which were eventually transplanted. Unavailability and exhaustion of members of the transplant team were frequent reasons for declining to use a potential donor. It is obvious that a redistribution of patients awaiting liver transplant to a more even spread among the various centres would lead to a more efficient utilization of all available organs.

It is quite possible, therefore, that five or six Canadian centres will be necessary to meet the eventual demand. These centres should be reasonably well scattered geographically in order to minimize the social cost incurred by patients and their families who may have long distances to travel both for the operation and in the long post-operative phase. Children's transplants would ideally be carried out in pediatric hospitals accustomed to dealing with chronically ill children and their families. Because of the small number of potential pediatric recipients (fifty or sixty per year), more than two such centres will not likely be necessary.

Requirements of a liver transplant centre

The well organized participation of numerous medical and para-medical disciplines is necessary to ensure the success of any liver transplant program. Good working relationships between gastroenterologists, surgeons, anaesthetists, intensivists, the transfusion service, infection disease specialists and organ procurement services are essential. In pediatrics, participation of behavioural and developmental services as well as occupational therapy, physiotherapy and nutritionists is necessary to support and study the development of the child in the post-transplant phase.

Skilled transplant coordinators facilitate the efficient transport of patients and their families to the transplant centre before and after the operation and are instrumental in orchestrating the follow-up procedures once patients are discharged.

The establishment and location of liver transplant centres must be agreed upon at both national and regional levels of government, and extra-funding allocated to support the added costs.

Donor procurement

Until a method of preservation which will allow livers to be stored for longer periods of time is discovered, the successful outcome of a liver transplant hinges upon the quick and atraumatic harvest of the organ from the donor, and its implant into the recipient within eight to twelve hours of its removal.

Once a potential donor is identified, prospective recipients are selected solely on the basis of size, bold type, and degree of urgency. No immunological criteria such as HLA matching or presence of preformed recipient anti-donor antibodies have proven to be of significance in determining allograft survival.

Once a patient has been declared brain dead and consent for organ donation obtained, the suitability of a liver for transplantation is determined by relatively simple means. Ideally, liver donors should be less than 45 years of age and have no history suggestive of hepatobiliary disease. Liver enzymes and serum bilirubin should be normal. In cases where liver function tests are abnormal but improving, the liver may still be considered suitable for transplantation.

The task of maintaining potential organ donors in optimal physiological condition and organizing the necessary tests to adequately assess the function of extra-renal organs has greatly increased the effort expended by intensive care personnel caring for critically ill patients. This extra work must often take place in the face of under-staffing and bed shortages. The cooperation of intensive care medical and nursing staff is important in order to meet the universally increased need for kidneys, livers and hearts. One of the major roles of organ procurement services and transplantation surgeons is to offer guidance in the management of potential donors and at the same time maintain cordial relations with intensive care doctors and nurses by recognizing the special needs of the I.C.U. The advent of extra-renal organ transplantation has led to changes in the way organs are removed from the body. For removal of the liver and kidneys, the liver is first carefully dissected out with particular attention to the arterial supply which may vary considerably. Starzl has elaborated the principle of pre-cooling, whereby the splenic vein is cannulated and infused with cold physiological electrolyte solution thereby cooling the liver while the final stages of the dissection are completed. The lower infrarenal aorta is then cannulated, and in quick succession, the final steps take place: clamping of the supraceliac aorta, rapid infusion of cold solution through the portal vein and lower aorta, and exsanguination through the inferior and superior venae cavae. When skillfully done, these steps result in rapidly cooled, bloodless livers and kidneys which can then be rapidly removed and stored in iced preserving solution. This so called "in

situ perfusion" method of organ harvesting can also be modified in order to allow removal of the heart. Studies of the post-transplant function of kidneys harvested by this method have shown equally good results when compared to the more traditional methods of "ex vivo" renal perfusion. Collin's solution or similar high-potassium, high-carbohydrate, phosphate-bufferred solutions remain unchallenged as currently used liver preservation solutions, although experimental work using cell membrane stabilizers or free radical scavengers to prevent cellular swelling and re-perfusion injury have yielded promising results.

Starzl has advocated the routine harvesting of the distal aorta and iliac arteries in order to enable the construction of arterial conduits should primary hepatic artery anastomosis prove impossible. The Minnesota group has modified this procedure for infants by dissecting the arterial supply to the liver in continuity with the coeliac trunk and thoracic aorta for later use in the arterial reconstruction.

Cooperation between teams at different liver transplant centres in the procurement and exchange of livers remains minimal, therefore requiring members from the recipient centre to travel, in most cases by air transport, to where the donor is located. The short cold ischemia time tolerated by the liver requires that the team dispatched to harvest the liver keep in frequent touch with the home hospital to advise them of their progress. Once a liver is deemed suitable for transplantation, the recipient team begins the task of mobilizing the diseased organ and is ready to remove it once the new liver is brought into the operating room. The final preparation of the liver takes place while it is bathed in iced electrolyte solution with none of the attendant risks of warm ischemia.

Recipient operation

The indications for liver transplantation have evolved in the last twenty years. In children, biliary atresia and the inborn errors of metabolism account for the great majority of cases of pediatric end-stage liver disease. In adults, primary biliary cirrhosis, cirrhosis from non A — non B hepatitis and sclerosing cholangitis are the commonest indications for the operation. Liver replacement for malignant disease has proved to be largely a futile exercise because of the overwhelming tendency of tumours to recur within six months of the operation. Tumours with fibrolamellar histology are exceptions to this rule, and result in a lower incidence of recurrence.

All prospective recipients undergo an extensive work-up for assessment of their liver function, biliary and venous anatomy, and their immunological status. Ideally, recipients would be less than 55 years old and have no extra-hepatic foci of sepsis. Portal vein thrombosis remains an absolute contraindication for the operation. Patients with malignant diseases are carefully screened for metastases.

Starzl and others have stressed that the often very long waiting period for appropriate liver donors can result in significant deterioration in the state of prospective recipients. This is especially true with small children, where over half the patients under eight kilograms die while waiting for liver. Therefore, experienced centres have developed a policy of earlier intervention with the double aim of increasing the chances of finding a suitable liver as well as of operating on a patient who can better withstand the rigours of the operation.

The recipient operation starts by the laborious task of mobilizing the diseased liver. In cases where previous surgery has taken place, this phase may be particularly difficult. One of the most significant changes in the technique of the recipient hepatectomy has been the development of a non-heparin dependent veno-venous bypass system using a centrifugal pump. Although the necessity for bypass has not been universally accepted, the experience in Pittsburgh strongly suggests that its implementation has resulted in shorter operating times, lessened blood loss and a decrease in post-operative renal failure. This technique has not proven necessary in small children, and the Pittsburgh approach has been to use it in recipients weighing over 40 kilograms.

Once the old liver is out, the new one is sewn in as rapidly as possible by the anastomosis of the supra-and infra-hepatic venae cavae and of the portal vein. Venous flow is hence restored and the arterial anastomosis can then be completed.

The long arduous task of obtaining hemostasis then begins. Bleeding may be compounded by a profound coagulopathy based on clotting factor deficiencies which arise during the anhepatic phase.

The biliary anastomosis favoured in adults by most centres is the choledochocholedochostomy over a T-tube; however, Calne still prefers to construct a conduit using the donor gall bladder to bridge the distance between the donor and recipient common bile ducts. In children, the small size of the ducts makes primary anastomosis more difficult and a Roux-en-Y choledochojejunostomy is usually carried out. Frequent complications such as leakage may occur at the biliary anastomosis, and whenever possible, intra-operative cholangiograms are obtained to insure the integrity of the anastomosis.

POST-OPERATIVE PERIOD

1. Immunosuppression

Liver allografts occupy a privileged position among transplantable organs. It has long been known that liver allografts in pigs may survive indefinitely with no

immunosuppressive therapy. Although a refection response is usually mounted within the first ten days after transplantation, it often resolves spontaneously, and a state of tolerance is established with respect to the graft. Liver transplantation between certain strains of rats disparate for the entire major histocompatibility complex (MHC) results in spontaneous and uniform long term allograft survival. This form of allograft enhancement has been shown by Kamada of Cambridge to be specific for the donor haplotype, and it has been suggested that there may be deletion of donor-reactive lymphocyte clones as a consequence of the release of large quantities of soluble MHC class I antigen into the recipient circulation.

In humans, there have been no reported cases of long term liver transplant survivors without immunosuppression. The unique properties of liver transplants are apparent, however, even in the clinical setting. Hyperacute rejection, even in the presence of preformed anti-donor antibodies, has never been reported, and no discernable effect of HLA -matching on allograft survival has become apparent.

Prior to 1980, corticosteroids and azathioprine were the twin pillars of clinical immunosuppression. The serious side-effects of steroids in children (including growth retardation) led Calne at one time to express great reluctance in performing liver transplants in the pediatric age group. This philosophy is reflected in the very small number of children in the Cambridge series.

The introduction of cyclosporine to clinical liver transplantation in 1980 has been heralded by Starzl as the single most important advance leading to the current high survival rates. Cyclosporine is produced from the fungus Tolypocladium inflatum and its first clinical application by Calne in renal transplants took place in 1978. Unlike other immunosuppressive agents, cyclosporine is neither cytotoxic nor a marrow suppressant. It appears to act chiefly by inhibiting the activation of T-helper cells and thus interfers with development of T-cell dependent cellular and humoral immunity towards new antigens. Evidence has also been obtained to suggest that, while preventing the development of cytotoxic mechanisms, the generation of T-suppressor cells is not opposed.

The most important sequela of cyclosporine usage has been its steroid-sparing effect. This has been particularly valuable in pediatric transplantation. The great number of immunosuppressive protocols which are now in use testify that there is no consensus on how cyclosporine is best used and which drugs can be added as immunosuppressive adjuncts. Starzl favours the early implementation of high-dose intravenous cyclosporine with a gradual switch-over to the oral drug once the production of bile in the new liver improves to permit sufficient absorption. Intravenous methylprednisolone in high doses is quickly tapered to maintenance levels. Blood or serum concentration of cyclosporine is closely monitored by means of a radioimmunoassay (RIA) and, because of the drug¢s nephrotoxic effects, serum creatinine is measured daily. The Cambridge group favours the early use of prednisone and azathioprine until good post-operative renal function is established and only then implementing oral cyclosporine. The Cambridge experience suggests that the intravenous form of the drug is the one most likely to cause renal dysfunction. Krom of the Groningen group has avoided the use of cyclosporine altogether, favouring the use of azathioprine and steroids.

Cyclosporine has also been implicated in causing hepatic dsyfunction, but there is no clear evidence to support this claim. Anecdotal reports do exist, however, suggesting that cyclosporine may be a cause of increased bilirubin post-operatively. Other side effects include tremors, gingival hyperplasia and hypertension.

Most centres have modified their approach to immunosuppression by eliminating or reducing the use of cyclosporine if preoperative renal function is poor. Azathioprine and a limited prophylactic course of anti-lymphocyte globulin (ALG) are used instead. ALG contains antibodies directed against human T-lymphocytes and works by reducing the number of mature T-cells in the circulation, decreasing T-cell proliferative function, and possibley inducing non-specific T-cell mediated suppression.

Evidence of rejection usually appears by the fifth to seventh post-transplant day and is signalled by an increase in serum bilirubin and transaminases. Acute cellular rejection usually responds to bolus therapy with intravenous steroids. if such therapy does not produce a reversal in the signs of rejection, a therapeutic course with ALG can be instituted. More recently, a monoclonal antibody reactive to the CD3 receptor on human lymphocytes has become available for the treatment of acute rejection. OKT-3 (TM) (Ortho Pharmaceutical Ltd.) is a pan-T cell reactive antibody which causes the elimination of all CD3-positive cells within minutes of its administration. It has been proven very useful in the treatment of acute rejection both in kidney and liver transplantatin, although sustained unresponsiveness is not maintained after discontinuation of the antibody. Its advantages over ALG are a decrease in the incidence of side effects and a narrower target range resulting in less interaction with red cells, platelets, serum proteins, B lymphocytes, and neutrophils. Because OKT-3 (TM) is raised in mice, its usefulness is severely limited by the development of anti-murine antibodies.

2. Post-operative complicatons: Early

Bleeding and arterial thrombosis are the two most likely complications to jeopardize the life of the patient in the first few days following surgery. Although meticulous hemostasis and the reversal of coagulopathies with

fresh frozen plasma, cryoprecipitate and platelets has diminished the problems from bleeding, anastomotic complications in the hepatic artery can still result in allograft infarction with the subsequent death of the patient unless a replacement liver can quickly be found. Arterial thrombosis has been a problem particularly troublesome in children because of the small calibre of the vessels. This has led to the practice of prophylactic anti-platelet therapy with acetyl-salicylic acid in some instances. Arterial thrombosis may, however, result in a less dramatic deterioration, and present with persistent intrahepatic abscesses refractory to antibiotic therapy and necessitating a repeat liver transplant.

Respiratory failure from pulmonary oedema and hypertension from fluid overload, steroids and cyclosporine are common early post-operative problems and usually respond to ventilatory support, diuretics, and aggressive anti-hypertensive management.

Bacterial sepsis is less common with the prophylactic use of broad-spectrum antibiotics, but may signal the presence of a biliary anastomotic dehiscence.

Fever, jaundice and elevated liver enzymes in the first week may represent vascular thrombosis, sepsis from a bile leak or early rejection. An aggressive diagnostic approach is necessary to implement the appropriate therapy. Ultrasonography is useful in determining the state of the portal vein and hepatic artery in children, but angiography is often necessary to rule out thrombosis in adults. A T-tube cholangiogram will clearly demonstrate the integrity of a biliary anastomosis to rule out a bile leak, but in children with no indwelling biliary catheters, a radionuclide excretion scan can be helpful. rejection can be diagnosed from a percutaneous liver biopsy. although the clinical picture and the response to therapy is more important in gauging the presence and severity of rejection than the appearance of a liver biopsy.

Late

Rejection continues to be an ever-present threat for the long term, although there is evidence to suggest that an adaptive process occurs between the host and the graft to decrease the chances of rejection. After the first year following transplantation, the survival curves in children and adults flatten out and the chances of losing the allograft to rejection decrease. Cyclosporine and steroid dosages are gradually decreased and the prednisone may be stopped completely. Successful discontinuation of all immunosuppression, unfortunately, has never been reported.

Infections with opportunistic organisms represent the major post-operative late complication. Eighty-five percent of patients in the Pittsburgh series exhibit evidence of viral infection. Herpes simplex and zoster infections often represent reactivation of latent disease. Acyclovir has proven extremely effective in treating symptomatic herpes infections, and some reports advocate its use in a prophylactic manner. Cytomegalovirus (CMV) represents a more threatening problem due to the unavailability of effective therapeutic agents. CMV hepatitis can closely resemble an episode of rejection, but the treatment requires a reduction of the immunosuppression. In addition to hepatitis, CMV can cause pneumonitis, leukopenia, thrombocytopenia, and, in the long-term, chorioretinitis. Measures to control and reduce the severity of CMV infection include passive immunization with CMV hyper-immune globulin, screening of blood and blood products for CMV, and screening of potential donors for anti-CMV antibodies. These preventive measures bear particular significance to the pediatric recipient who has had no prior exposure to CMV and may be infected for the first time in the immunosuppressed state. Prophylactic measures obviously will have no effect on the reactivation of latent disease in previously infected recipients.

Pneumocystis carinii and Nocardia may be prevented by administration of prophylactic trimethoprim-sulfamethoxazole.

Fungal sepsis carries a particularly high mortality. Strict attention to preventive measures such an removal of central lines and urinary catheters, prophylactic use of oral nystatin and prompt institution of amphotericin B in cases of candidiasis without fungemia will help to minimize the adverse consequences. Infection with Aspergillus, however, carries a mortality approaching one hundred percent. Reactivation of Hepatitis B virus has been reported to result in the virtual destruction of new transplants. Post-operative treatment of HBV Ag positive patients with Hapatitis B immune golbulin may decrease the incidence of recurrent severe hepatitis. Active immunization against HBV of all prospective recipients will also help to reduce the severity of this problem in the post-operative period.

Re-Transplantation

Thirty percent of current recipients in the Pittsburgh program are rceiving their scond or third livers. half of the retransplants are for liver failure due to chronic rejection and take place months or years after the first transplant. The other fifty percent of the retransplantations occur in the relatively acute post-operative period to treat allograft infraction due to arterial or portal vein thrombosis or for primary non-function most likely due to an unrecognized problem in the donor liver or a harvesting injury. Allograft failure from primary nonfunction or arterial thrombosis will usually result in the death of the patient unless a new liver can quickly be found. At the present time, no form of clinically applicable artificial liver can be used.

Long term results

Throughout the 1970's, one-year survival in Denver and Cambridge was approximately 30%. Children lived longer than adults, and patients with non-malignant disease did better than those with malignancy. Since 1980, Starzl has reported a remarkable improvement in the one-year survival which is now approaching 80-85%. He has attributed the increased success rate to better immunosuppression with cyclosporine, improved methods of organ procurement, implementation of the veno-venous bypass, and availability of retransplantation to treat allograft failure. Survival rates in other centres, while not as high, nevertheless represent remarkable improvements from those obtained in the pre-cyclosporine era. One year survival figures since 1980 in Cambridge have been reported to be approximately 50%. Hannover and Groningen currently report one-year survival rates of 60 to 70%. Current four-year actuarial survival in Pittsburgh is almost 80% for children and 50% for adults.

Liver transplantation for primary or secondary malignancy has yielded disappointing results. While transplantation for fibrolamellar hepatomas has yielded acceptable results with recurrence rates of 50%, the rate of recurrence with other forms of liver tumours is quite high at over 80%. Moreover, recurrences usually occurr in less than one year after transplantation. In Pittsburgh, of 23 patients with non-fibrolamellar carcinoma, only five lived for as long as a year at which time all but one had known metastases.

Survival in patients whose livers were transplanted for non-malignant disease but whose livers contained incidental malignancies has been excellent in Starzl's experience. Twelve of 13 patients are still alive four months to 16 years after surgery.

The excellent current survival in children transplanted for liver failure due to biliary atresia has prompted Starzl to suggest a more selective use of the Kasai portoenterostomy, Results of liver transplantation in children with biliary atresia have not been reported to be as good as those in children with metabolic liver disease. The reasons for this are partly due to the increased blood loss, and to the considerably more challenging technical difficulties which have to be overcome because of the extensive and often repeated surgery in the right upper quadrant and porta hepatis. A more selective approach in using the Kasai procedure would spare some infants unnecessary surgery and improve their chances of survival after a liver transplant. Unfortunately, there are no reliable predictors of which children will improve after a portoenterostomy. It is unreasonable at this point to suggest transplanting all infants with biliary atresia because of the scarcity of suitable donors in this age group.

Areas of future research

Improved methods of preservation for harvested livers would increase the time available to find suitable recipients, and allow for more flexibility in scheduling operating room time without necessarily cancelling electively booked cases. Current research into improved methods of preservation include prevention of reperfusion injury by elimination of oxygen-derived free radicals and stabilization of cellular and sub-cellular membranes with agents such as Co-enzyme Q, prostaglandins, and heavy water (D_2O).

Rejection and opportunistic infections remain the chief causes of patient mortality. Current methods of immunosuppression greatly reduce immunity against microorganisms as outlined above. The goal towards which immunotherapy should be directed is the suppression of reactivity towards donor antigens while preserving the ability to mount an immune response against invading pathogens. The only currently used form of donor-specific immunosuppression takes place in renal transplant programs which deliberately transfuse prospective recipients with donor blood prior to a living-related donor transplant. This policy has resulted in a one-year allograft survival of over 90% as reported by Opelz in Heidelberg and Leivestad in Oslo.

Although a great deal of animal work supports the theory of MHC antigen induced donor-specific immunounresponsiveness, the practical applications of this principle in clinical transplantation remain a long way off.

Conclusion

Liver transplantation has ceased to be an experimental procedure, and is now an established method of treatment for patients with end-stage liver disease. Well over a thousand liver transplants have been done worldwide, and current overall one-year actuarial survival rates in patients receibing livers for nonmalignant

Med-Chem Laboratories Limited
BIOCHEMISTRY HEMATOLOGY IMMUNOLOGY RADIOIMMUNOASSAY
PARASITOLOGY MICROBIOLOGY SEROLOGY CARDIOLOGY NUCLEAR MEDICINE

FULL LABORATORY SERVICE INCLUDING:

* Ontario-wide report delivery and specimen pick-up in refrigerated cars
* House-calls available on request for specimen taking and ECG's
* STAT service available on most tests
* Results ready in 24-48 hours on most tests
* Customer Service Department for your special needs and inquires open 9:00 a.m. to 9:00 p.m. weekdays

QUALITY, CARE AND SERVICE

4500 Sheppard Avenue East, Suite G, Agincourt, Ontario M1S 3R6
Telephone (416) 291-8186 Toll Free 1-800-268-5517

disease vary from 50 to 85%. Children, in particular, have lower perioperative mortality and higher overall survival than their adult counterparts.

Many of the technical problems of earlier days have been resolved, and the main causes now of the morbidity and mortality in the postoperative period are opportunistic infections and chronic rejection. Primary nonfunction and arterial thrombosis, however, still present significant causes of mortality within the first postoperative month.

The quality of life after liver transplantation has been and continues to be a matter for debate. In adults transplanted in Pittsburgh, over 80% of patients who have survived for more than a year have returned to their former occupations. In children, over half the survivors exhibit catch-up growth and most of the rest resume growth at normal rates and do not fall any further behind their expected growth curves. Only a small proportion continue to lose ground developmentally.

Patients and their families must be carefully counselled preoperatively to allow them to make the decision regarding transplantation with as few illusions as possible. Life after liver transplantation implies exchanging a form of lethal liver disease for a more chronic condition needing long-term medical supervision and, possibly, life-long medication with all the attendant risks of immunosuppression. There is no doubt that most survivors of the operation have no regrets about the decision; however, those facing the prospect of liver transplantation either for themselves or for their children, will not find that decision an easy one. Psychiatric and social support for these patients and their families must be considered as essential to the long term happiness of these patients as their physical care.

Liver transplantation programs, as no other medical endeavour before them, depend on a coordinated multidisciplinary approach to patient care to achieve the current levels of success.

Suggested Reading on Liver Transplantation

1. Starzl T.E.: Experience in Hepatic Transplantation. Philadelphia, W.B. Saunders, 1969.
2. Calne R.Y. (ed): Liver Transplantation. New York, Grune and Stratton, 1983.
3. Simmons R.L., Finch M.E., Ascher N.L., Najarian J.S. (ed): Manual of Vascular Access, Organ Donation, and Transplantation. Comprehensive Manuals, of Surgical Specialties. New York, Berlin, Heidelberg, Tokyo, Springer-Verlag, 1984.
4. NIH Consensus Development Conference on Liver Transplantation. Hepatology 4:15 - 1105, 1984.

THE UNIVERSITY OF TORONTO

MEDICAL BOOKSTORE

Textbooks for all subjects

Comprehensive reference books
and general interest titles.

Complete review manuals in Medicine and Nursing

- Ask for our free catalogue
- free special order service

OPEN: MONDAY — FRIDAY 8.45 am — 6.00 pm
SATURDAY 11.00 am — 5.00 pm

LOCATION: 214 COLLEGE STREET
(COLLEGE & ST. GEORGE)

TEL: 586-7913

A Severe Hand Injury From An Ancient Muzzle Loading Cannon:

Modern Management of the Severely Injured Hand

John L. Semple, B. Sc., M.D.

It is rare in a modern medical career to be confronted with an injury in a young man from a muzzle loading cannon. Dramatizations by movies, television, historical novelists and artists have all given us an inaccurate Hollywood-depicted version of what kind of injuries were sustained during ancient battles. There is a classic scene where the hero sustains an injury to his hand or arm while leading a charge into almost point-blank cannonfire. Recoiling, he clutches his arm and the magnitude of the wound is reduced to a grimace, a wink and a small red spot on the sleeve of his tunic. As he picks up his saber (with the injured hand) and runs off into the smoke of the battle, we are left to marvel at the wonderfully rapid wound healing and resiliance of movie stars and the apparent insignificance of ancient weapons. The reality of such a devastating injury combines a high velocity shattering force, severe gunpowder burns (further damaging devitalized tissue) and a high degree of foreign body contamination.

In ancient battles, field surgeons had little choice in management of such injuries. There was no thought of possible salvage of the hand since, in the absence of antibiotics and modern debridement techniques, gangrene and infection set in very quickly. Amputation of the limb was the most common treatment (3).

Having the opportunity to treat such an ancient injury under modern conditions, underlines the important principles that have been with modern surgical techniques, antibiotics and extensive support facilities. It is often possible in this modern age to salvage the most severely mangled hand and return it to a functional unit.

Discussion of the following unfortunate case of a young gunner from Fort York will allow us to review the modern principles and approaches to a severely injured hand.

On the evening of July 3rd, 1985, there was a performance of Tschaikowsky's 1812 Overture (Fig. 1) at the Ontario Place in Toronto. Our patient was a right-handed 22 year old male who, as a member of the Fort York Guard, was attending and loading a cannon which was used for the special effects during the finale of this musical performance. The patient had worked as a summer student at Fort York Guards for the past two years. During the winter season he attended George Brown College as an art student.

The cannon on which the patient was attending was an authentic brass antique, muzzle loading Howitzer type cannon, vintage 1859 (Fig. 2). The cannon had been fired once and upon reloading the cannon for the second shot, the charge exploded prematurely. At the time the charge went off, the patient was standing in front of the cannon, ramming the charge into the bottom of the barrel holding a wooden ramrod in his hands (Fig. 2). According to witnesses, there was a flash, the patient was knocked down a small incline and was quickly attended to by bystanders. He was rushed to St. Joseph's Hospital and then immediately transferred to the Ross Tilley Burn Centre at the Wellesley Hospital.

The initial assessment at the time of his arrival included: gunpowder flash burn to the face, traumatic amputation of the right hand at the wrist, compound, comminuted fractures and massive soft tissue injury to the dorsum of the left hand, and possible inhalation injury.

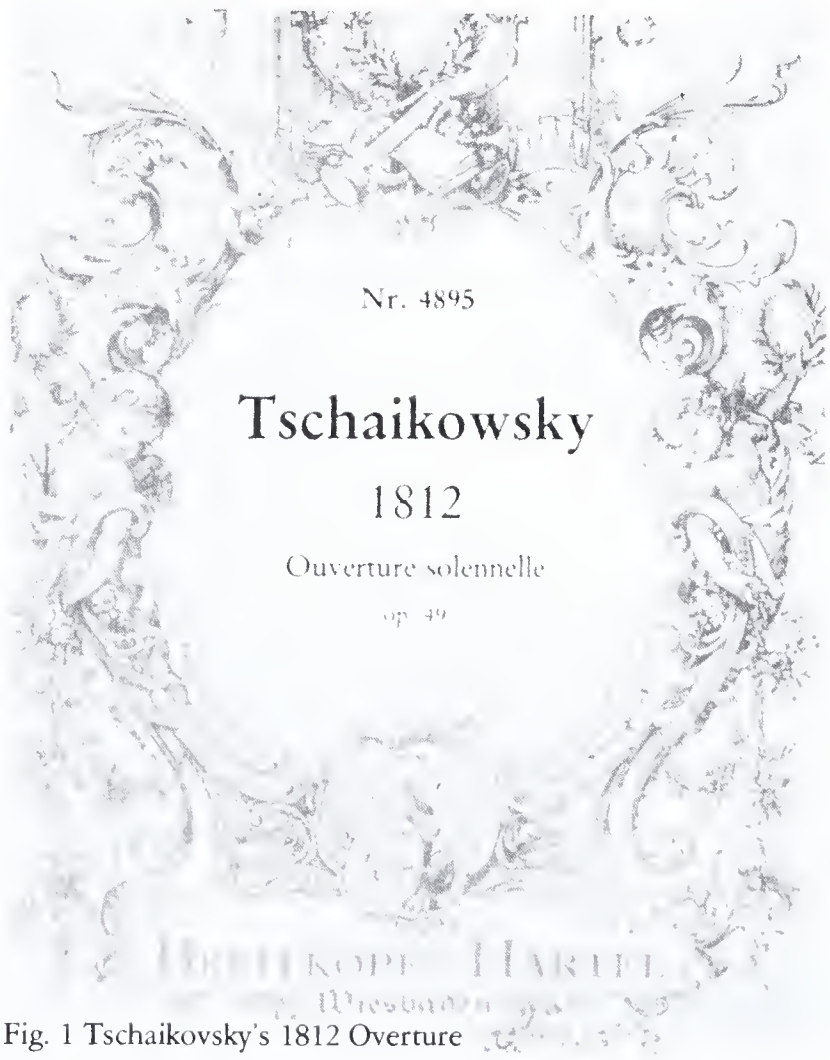


Fig. 1 Tschaikovsky's 1812 Overture

Evaluation It is mandatory to understand and appreciate the full extent of the initial injury to all the different tissues which make up the hand. Great care must be taken to assess the viability of these tissues since early decisions regarding the preservation in whole or in part of theseverely injured hand determine the course of reconstruction, as well as the patient's psychological and physical expectations. Examination of the severely injured hand must include the whole patient to rule out other significant associated injuries in other vital body systems. These other systems, if injured and life-threatening, should take priority over the hand injury.

Pre-existing medical conditions must be established such as diabetes mellitus, atherosclerosis, collagen vascular disease and blood dyscrasias. Drug allergies and prior tetanus immunization is important in the organization of antibiotic therapy. The patient's age, occupation,dominant hand and history of previous injury to the hand must be taken into account. Understanding the actual mechanism and nature of the accident is vitally important in estimating the extent of the injury and planning the treatment.

The patient was a 22 year old, right handed male art student who prior to the accident was in excellent health. On initial examination the patient's face, chest and arms were covered with black gunpowder burns. Black gunpowder is known to continue burning at extremely high temperatures as it leaves the barrel of the cannon.

Both hands were in the line of fire of the barrel as the patient rammed the charge into the depth of the barrel (Fig. 2). Had the patient been standing directly in front of the barrel the accident would likely have been fatal. The right hand for all intents and purposes had been blown away leaving a mangled arrangement of carpal bones and shredded tendons.

Examination of the left hand revealed a complex injury involving the shattering high velocity injury of the blast, the deep and penetrating gunpowder burns and extensive contamination with foreign body particles of wood splinters from the exploded ramrod.

Examination

The examination of the injured hand must be carried out with meticulous technique under sterile conditions. The entire extremity should be assessed and will often require a general anaesthetic. Prior to transporting the patient to the O.R., radiograms of the injured extremity are mandatory. These are helpful, not only in assessing fractures and joint dislocations, but also in examining the soft tissues for the presence of gas and foreign matter and for the extent of swelling. If replantation is anticipated, the amputated part must also be radiographed.

Blood for a complete blood count, chemistry profile and type-and-cross match should be drawn during the initial assessment.

Fig. 2 The method used to ram the charge into the end of the cannon. As the ramrod travels down the barrel the left hand comes away from the barrel — the point at which the accident happened.

Close examination and evaluation should be carried out under sterile conditions in the operating room, with magnification, anaesthesia, adequate lighting and proper equipment. Wound cultures, both aerobic and anerobic, should be taken from different sites of the wound. While assessing the would, meticulous debridement, irrigation, and removal of foreign particles is carried out. In crush injuries, burns and high-velocity accidents, it is also important to be aware of the possibility of development of a compartment syndrome. This may require surgical release of the carpal tunnel and/or interosseous muscle compartments. As part of the initial management intravenous broad-spectrum antibiotics should be used.

If replantation of an amputated part is anticipated, this should also be debrided, cleaned, wrapped in saline-moistened sponges, and placed in a sterile polyethylene bag which is stored in ice solution at 4°C.

Hand injuries can be grouped into the following categories:

Guillotine: These injuries have the most favourable prognosis for replantation. The hand is sharply and cleanly incised with minimal tissue damage.

Crush: These injuries have diffuse tissue damage which is often more extensive than revealed by the initial assessment. Sequential evaluation and debridement is essential to determine viability. Crush injuries have a poor prognosis and the healing is complicated by excessive fibrosis and edema secondary to the diffuse

tissue destruction.

Avulsion: These injuries are caused by a tearing force that literally rips the injured hand apart. There is often tearing of the neurovascular bundles, with avulsion of the tendons from the musculotendinous junction. Problems arise in determining vascular integrity since there is often multilevel injury with tendency to late thrombosis. These injuries also have a poor prognosis.

High Velocity: The extensive shattering force of a high velocity injury sustained in an explosion or gunshot wound is transmitted to distal and proximal tissues leading to delayed injury. There are often extensive areas of devitalized tissue adjacent to the actual wound.

In severe, mutilating hand trauma, some or all of these types of injuries may be present. Burns, chemical damage and heavy bacterial contamination may complicate an already devastating injury.

The patient's right hand had been lost at the time of the explosion and had been reduced to a mangled arrangement of carpal bones and shredded tendons. There was no bleeding from the distal stump and radiograms revealed fractures of both distal radius and ulna, as well as of the mid-shaft of ulna. Since there was no tissue to work with here, the only course of treatment was that of a revision amputation.

The left hand was intact but had suffered a severe complex injury. There was significant soft tissue loss to the dorsum of the hand, tendons and bone fragments being visible at the base of the wound. Deep and extensive powder burns were present up to the mid-forearm. There were wooden splinters from the shaft of the ramrod deep in the wound around the fractures and in the joint spaces. The witnesses at the site of the accident stated that the actual pole of the ramrod, which the patient was holding, had splintered into small fragments during the explosion. Some of this debris has penetrated the dorsum of the hand at high velocity. The skin and soft tissue on the volar aspect of the wrist and hand were intact. A radial pulse was present and there was some sensation in the small and ring fingers. Roentgenograms of the left hand showed multiple fractures, including thumb and index finger metacarpals (Fig. 3). The proximal phalanges of the index, long and ring fingers also had multiple fractures. The long finger proximal phalanx was severely comminuted.

Fig. 3 AP view roentgenogram of left hand on admission showing fractures through the metacarpals of the thumb and index finger and the proximal phalanges of the index, long and ring finger. Note the soft tissue swelling.

Treatment

A treatment plan is formulated in a logical manner, keeping in mind the six parameters suggested by Midgley and Entin[6]: length, strength, position, stability, mobility and sensibility. Careful debridement, irrigation and removal of foreign particles is followed by skeletal fixation, revascularization (if required), soft tissue repair and coverage (temporary or permanent). During this process, it must be decided where the maximum effort should be directed in terms of salvage, reconstruction and the ultimate function of the hand. Amputation of a part or the whole hand is an accepted form of treatment when the damage is too extensive.

Skeletal Fixation: Bony fixation must be attained before soft tissue repair can be carried out. The goals are maintaining length and early motion. With the advances of internal fixation using interosseous wires, screws, mini-plates and Kirschner pins or wires, early motion can usually begin in 2-3 days. External fixation, bone grafting, and sometimes joint spacing may be required.

Soft Tissue Repair: Repair of soft tissue structures such as tendons, ligaments, nerves and vessels, is undertaken after using a non-absorbable (permanent) suture. If skeletal stability allows early motin, this is also important in the ultimate function of the tendons.

Ligaments are repaired to provide stability to the joints. Primary repair of the nerves is carried out if there is no loss of nerve length. If there is loss of length, nerve grafting may be required in the future. External neurolysis may be required in crush or high velocity injuries to reduce further damage by edema formation. Nerves to amputated parts are sharply trimmed back and, if possible, buried in the shaft of a long bone or in an interosseous muscle to prevent painful neuromas.

Closure: Wounds are ideally closed, primarily, without tension. However, with extensive injury and subsequent debridement, substantial skin defects may be left. The concepts of adequate debridement and delayed primary closure have been emphasized in high velocity injuries. Healing by secondary intention encourages scarring and fibrosis and will compromise the ultimate goal of function. Choices for wound closure proceed in a routine order: simple closure, skin graft, local flap, distant flap, and free tissue transfer. Skin grafting is indicated if the graft can be placed on a healthy recipient bed. For small defects, local transposition flaps provide excellent cov-

erage. Distant flaps are indicated for large defects where there is exposure of the bone, joint, nerves, tendons or vessels. Large areas of exposed structures require distant flaps to provide adequate soft tissue coverage. Free tissue transfer may be indicated under certain circumstances. A split thickness skin graft may be used as a biological dressing until the wound is ready for definitive coverage.

Replantation and microvascular revascularization may be indicated in thumb amputations or when multiple digits are amputated. However, it is contraindicated when there is a severe crush injury, multiple fractures or degloving of the amputated part.

Splinting and Dressings: Following repair and coverage of the severely injured hand, proper dressing and protective splinting is required. Uninjured parts should not be splinted and motion should be encouraged.

Rehabilitation: Hand physiotherapists are consulted immediately following surgery to help the patient preserve what function remains in the uninjured portion of the hand and to help restore movement to the injured portions. The application of static and dynamic splints helps reduce the accumulation of edema and is also helpful in pain control. The physiotherapist is a key member of the team involved in returning the patient with a severe hand injury to a more functional state.

The left hand of our patient, therefore, had a complex injury including high velocity devitalization, thermal injury and severe contamination. These are all injuries poor prognosis and their combination presented a formidable challenge to the hand surgeon. Since the patient had lost his right hand it was crucial that the left hand be saved.

Sequential debridements were required to remove the devitalized and burned tissue. Many hours were spent removing wooden splinters from deep within the wound. Split thickness skin grafts were used for temporary coverage (Fig. 4) to protect the exposed tendons. With the multiple debridements and dressing changes, the wound appearance began to improve and no significant bacterial contamination was recorded. At this stage the patient's development and progress were reassessed. Since the patient required every option and treatment modality available including microsurgical free tissue transfer, he was transfered to the Toronto General Hospital, Division of Plastic Surgery under the care of Dr. B. Boyd and Dr. R.T. Manktelow. Here the patient underwent definitive bony fixation with AO miniplates providing excellent length and stability (Fig. 5).

At the base of the wound there was exposed tendon, bone, internal fixation plates and residual devitalized tissue (Fig. 6). This type of wound bed would not support a skin graft, while a standard groin flap would be quite bulky hindering the range of motion. The flap chosen for definitive coverage was a forearm flap (Fig. 7). This flap provided excellent coverage of the defect, minimal donor defect, and fascia at the flap base which allows unrestricted glide of the tendons. The flap was transposed distally on the radial artery and the distal blood supply maintained via an intact ulnar arterial system. The patient is an intelligent and well-motivated individual. With the support of the hand therapists, excellent results were obtained. The patient achieved an excellent range of motion (Fig. 8, 9), sensation in all digits, and had already began drawing prior to his discharge from hospital.

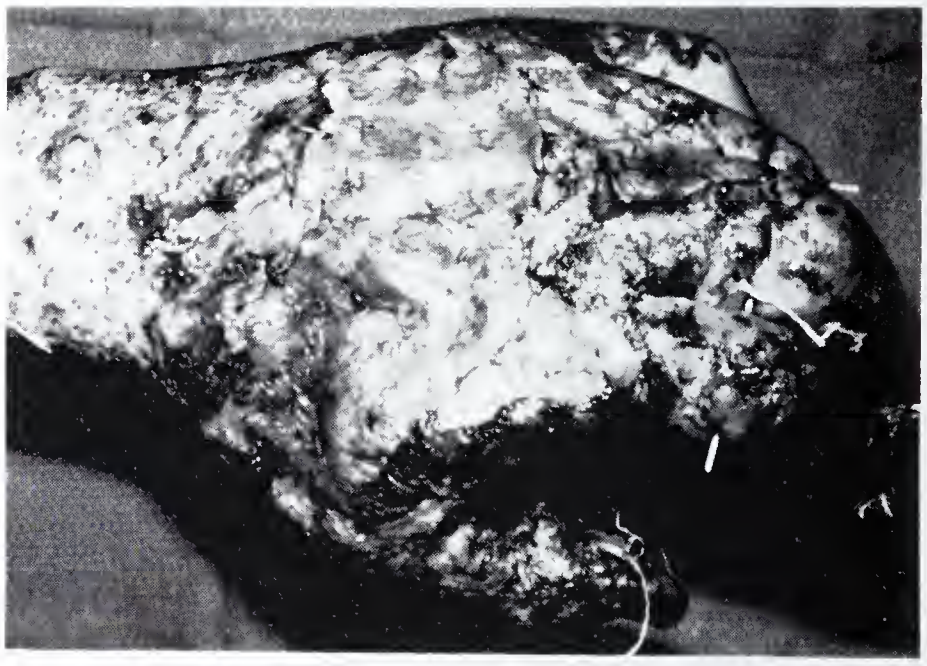


Fig. 4 Dorsal view of the left hand immediately after the first debridement, approximately 10 hours after admission. A split thickness skin graft is covering the tendons and acting as a biological dressing. Note the deep punctate gunpowder burns on the hand and wrist.

Fig. 5 PA view roentgenogram of the left hand showing definitive internal fixation using AO miniplates with good alignment.

Fig. 6 Actual size of the defect of the dorsum of the left hand showing burned tissue, exposed tendons, exposed AO miniplates and bone.

Fig. 9 This shows excellent grasp function and almost normal appearance of the hand.

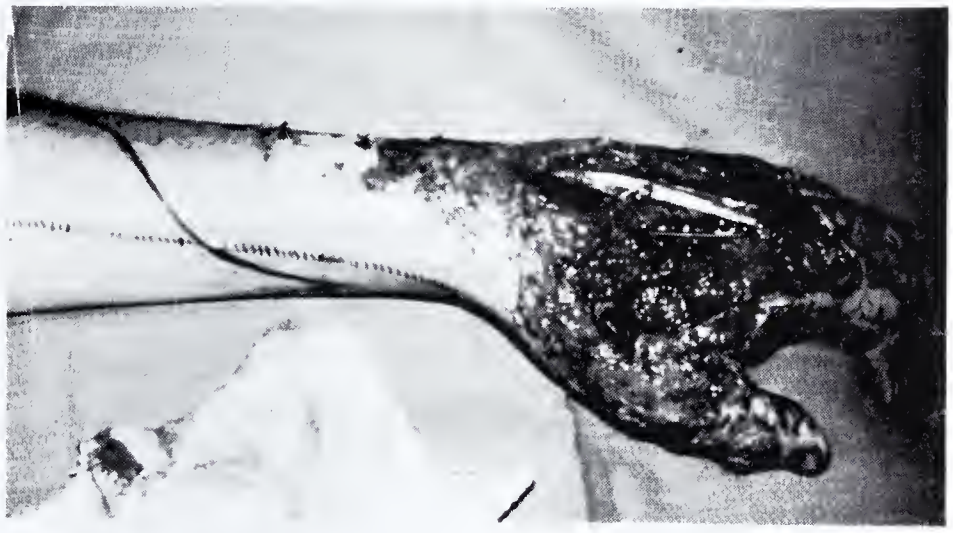


Fig. 7 This shows the flap design of the upper forearm prior to transposition. The material in the foreground is a tracing of the defect acting as a template for the flap design. The course of the radial artery is marked on the arm.

Fig. 8 The left hand with excellent function almost 2 months after the accident. Note the appearance of the flap and the burn scar hypertrophy around the flap edge and on the thumb.

Summary

The hand is a remarkably versatile instrument that performs complex and intricate functions. It is a sensory and proprioceptive system of ligaments, pulleys, tendons and joints, all of which depend on smoothly gliding surfaces for unrestricted motion.

By definition, a severely injured hand is one that has received extensive trauma in the form of crush, avulsion, explosion or thermal injury. In addition, foreign body contamination is common and a superimposed infection may further complicate the injury.

Wound healing in the severely injured hand is a complex matter. Scar formation is inevitable and is essential for repair to take place. However, the scar tends to unite all injured structures such that they are banded together as one unit (8). When a gliding structure such as a tendon adheres to an immobile structure such as bone, normal hand function is greatly impaired. Healing should be by primary repair if possible, since healing by secondary intention in hand wounds induces an amplification of the inflammatory response with a prolongation of the chronic inflammatory phase with increased edema, fibrosis and stiffness (1). It has been shown, however, that the connective tissue of adhesions and scars can be modified by motion and application of dynamic forces during the maturation phase of scar production. Collagen fibers can be reorientated from a random network to an organized thin band in which the fibers are parallel to the lines of tension. Early and constant motion helps to prevent excessive scar formation and development of adhesions, yet provides adequate strength in tendon repair.

The goals of treatment are to return the injured hand fully and rapidly to a functional state. This requires a coordinated team approach involving the reconstruc-

tive hand surgeon as well as extensive support facilities for rehabilitation. Presentation of this rather unusual case has allowed us to apply modern principles and surgical techniques to restore function to a hand which was severely injured by a cannon blast.

Acknowledgements

Dr. W.R.N. Lindsay, Division of Plastic Surgery, Wellesley Hospital Dr. J.B. Boyd and Dr. R.T. Manktelow, Division of Plastic Surgery, Toronto General Hospital

REFERENCES

1. Billmire D.A., Neale H.W., Stern P.J.: Acute Management of Severe Hand Injuries. Surg. Clin. North Am., 64(4), 1984.
2. Burkhalter W.B., Butler B., Metz W. et al: Experiences With Delayed Primary Closure of War Wounds of the Hand in Vietnam. J. Bone Joint Surg., 50A:945, 1968.
3. Greisman C.H.: Wound Management and Medical Organization in the Civil War. Surg. Clin. North Am., 64(4), 1984.
4. MacGregor I.A., Jackson I.T.: The Groin Flap. Br. J. Plast. Surg., 25:3, 1972.
5. Madden J.W.: Wound Healing: The Biological Basis of Hand Surgery. Clin. Plas. Surg., 3(1), 1976.
6. Midgley R.D. and Entin M.A.: Management of Mutilating Injuries of the Hand. Clin. Plast. Surg., 99(1), 1979.
7. Millard D.R., Cooley S.G.E.: A Solution to Coverage in Severe Compound Dorsal Hand Injuries. Plast. Reconstr. Surg. 49:215, 1972.
8. Peacock E.E.: Wound Repair, 3rd Ed. Philadelphia, W.B. Saunders, 1984.
9. Song R., Gas Y., Song Y., Yu Y., Song Y. The Forearm Flap. Clin. Plast. Surg. 9(1), 1982.
10. Wray R.C., Wise D.M., Young V.L. et al: The Groin Flap in Severe Hand Injuries. Ann. Plast. Surg. 9(459), 1982., Young V.L. et al: The Groin Flap in Severe Hand Injuries. Ann. Plast. Surg. 9(459), 1982.

GERIATRICIAN

The Riverdale Hospital — a 784 bed Long Term Care and Rehabilitation facility — is currently seeking to add a Geriatrician to the consulting medical staff.

Our hospital is located in downtown Toronto and is presently planning the redevelopment of the facility to create a regional geriatric centre.

The successful candidate will be dedicated to caring for the elderly in order to provide a continum of care in this community.
Please forward your resume to:

The Executive Director
The Riverdale Hospital
14 St. Matthews Road
Toronto, Ontario
M4M 2B5

(cont. from page 36)

References

1. Kannel, WB, Wolf PA, Verter J: Manifestations of Coronalry Disease Predisposing to Stroke: The Framingham Study. JAMA 250 (21): 2942-46, 1983.
2. Salonen JT, Puska P, Tuomilehto J, Homan K: Relation of Blood Pressure, Serum Lipids, and Smoking to Risk of Cerebral Stroke - A longitudional Study in Eastern Finland. Stroke 13 (3): 327-33, 1982.
3. Herman B, Schmitz PIM, et al: Multivariate Logistic Analysis of Risk Factors for Stroke in Tilburg, The Netherlands. Am J Epidemiol 118 (4): 514-25, 1983.
4. Stennermann GN, Hayashi T, Resch JA, et al: Risk Factors Related to Ischemic and Hemorrhagic Cerebrovascular Disease at Autopsy: The Honolulu Heart Study. Stroke 15 (1): 23-8, 1984.
5. Gross CR, Kase CS, et al: Stroke in South Alabama: Incidence and Diagnostic Features - A Population Based Study. Stroke 15 (2): 249-55, 1984.
6. SZatrowski TP et al: Serum Cholestrol, other Risk Factors, and Cardiovascular Disease in a Japanese Cohort. J. Chron Dis 37 (7): 569-84, 1984.
7. Rogers RL, Meyer JS' Shaw TG, et al: Cigarette Smoking Decreases Cerebral Blood Flow Suggestsing Increased Risk for Stroke. JAMA 250 (20) 2796-2800, 1983.
8. Bell, B.A, Ambrose J: Smoking & the Risk of a Stroke. Acta Neurochirurgia 64: 1-7, 1982.
9. Schmidex: Causes & Rates of Morbidity for Carotid Endarterectomy Based on 165 Rocedures in 150 Patients. Operative Techniques of Neurosurgery volume 2, 1982.
10. Sundt TM: Extracronial Occlusive Cerebral Vascular Disease, in Wilson CB, Hoff J. T. (eds): Current Management of Neurologic Disease. Churchill-Livingstone, 1980 p.p. 191-201.
11. Classification of Atherosclerotic Lesions. Report of a Study Group. Definition of Terms. WHO Rep. Ser. of 143:4, 1958.

Tumour Arthroplasty For Matastatic Disease Of The Proximal Femur

Richard W. McCalden, 8T6.

Pathological fracture is a frequent and unquestionably debilitating complication of skeletal involvement in metastatic disease. Approximately 70% of all pathological fractures within the appendicular skeleton occur in the femur, with 80% of these involving the proximal one-third.[5]

The aim of surgical treatment in these patients is to relieve pain and restore ambulation. Standard techniques of management include unipolar or bipolar hip arthroplasty or fracture stabilization using a variety of fixation devices.[3 5 11 12 20] If skeletal defects are extensive, augmentation with methylmethacrylate has been shown to greatly improve surgical results.[6 7] However, destruction of the proximal femur due to metastatic disease may, on occasion, result in so much bone loss that conventional forms of replacement and fracture stabilization are inadequate.

This retrospective study reports the results of proximal femoral replacement using a tumour prosthesis for the management of impending or pathological fractures due to metastatic disease. Unlike conventional total hip arthroplasty, the utilization of the tumour prosthesis requires reattachment of the hip abductor muscles. This study reports a new technique for excision of the proximal femur which facilitates the restoration of the hip abductors.

Materials

Over a ten year period (June, 1976 to October, 1985), 15 patients (16 hips) have been treated by proximal femoral replacement using a single type of tumour prosthesis (Protek-Mueller design). Surgery was performed on nine patients (10 hips) for pathological fractures resulting from metastatic disease. Four patients had suffered failure of previous stabilization of a pathological fracture and the remaining two patients were treated for an impending fracture through a large metastatic skeletal defect. Primary tumours included breast[7], renal cell[3], Prostate[2], lung[1] and one each of multiple myeloma and leiomyosarcoma. The patients with multiple myeloma and leiomyosarcoma both had multiple distant lesions. The ages of the patients ranged from 34 to 71 (mean — 60). The patient series is summarized in Table 1.

The charts and radiographs of all patients in the series were reviewed. The three living patients were personally examined and radiographed. Families of the deceased patients (12 patients) were contacted and questioned with regard to postoperative pain relief and ambulation.

Table 2. Patients' Best Postoperative Ambulatory Status

Status	No. of Patients
Bedridden	0
Bed to Chair	5
Household Ambulator (requiring walker or crutches)	5
Community Ambulator (requiring one or two canes)	5
Unassisted Ambulator	0
Total	15

Surgical Technique

As a number of surgeons were involved in the management of these patients a variety of approaches and techniques were used. The current technique, used in the last 4 patients, has evolved through increased surgical experience with the tumour prosthesis.

Preoperative planning is required to determine the level of femoral resection to ensure that the appropriate length of prosthesis is available and to assess the entire length of the femur so that all metastatic defects are suitably reinforced. Currently, an anterior lateral approach is employed developing the interval between tensor fascia lata and gluteus medius. The vastus lateralis is divided anteriorly to the level of the femoral resection. The femur is then exposed subperiostealy. At the level of the greater trochanter care is taken to preserve the continuity of the hip abductors, the periosteum over the trochanter and the vastus lateralis with its fascia.

The level of the femoral resection, determined preoperatively is measured distally from the intact greater trochanter, lesser trochanter, or the edge of the fracture. Removal of the proximal femur provides excellent exposure of the acetabulum which is prepared in the usual manner. The acetabular cup is positioned in 10 of anteversion and inclined 40 to the horizontal. Using the Knutchner flexible reamers the intramedullary femoral diameter is enlarged to 16 mm. Final reaming is done with a special reamer whose shape corresponds to that of the prosthetic stem. The size of the femoral prosthesis is determined preoperatively and confirmed at the time of trial reduction by the tissue tension and prosthetic stability. The prosthesis is

cemented in 10 of anteversion as guided by the bicondylar axis of the femur and the location of the linea aspera. Abductor reconstruction is facilitated by maintaining the continuity of the abductor mechanism consisting of the intact band of abductors, periostium and vastus lateralis. The intact abductor complex is then fixed to the prosthesis using a serrated plastic plate and screws. This is reinforced with sutures which approximate the gluteus medius to the tensor fascia lata and the vastus lateralis to itself.

Reviewing the entire series, the operative time averaged 2.8 hours and estimated blood loss averaged 1200 ccs. One of the three patients with metastatic hypernephroma, whose lesion had not been embolized preoperatively, experienced an intraoperative blood loss of approximately 4 litres. All patients received routine intraoperative and perioperative antibiotics.

Results

Survival: There were no perioperative deaths, with all patients surviving at least two months. Due to the extensive nature of the disease, only 11 patients (73%) survived 6 months and 6 patients (40%) survived 12 months. Of the 12 deceased patients, the mean survival was 13.3 months.

Pain Relief: Pain relief was considered significant if the patient required milder and/or frequent analgesics. Significant pain relief was obtained in 14 patients (93%). Of note, nine patients (60%) no longer required narcotic analgesics postoperatively. The one patient who failed to obtain pain relief had profound disseminated metastatic disease associated with spinal cord compression and had suffered an unrecognized prosthetic dislocation.

Ambulation: Ambulation was restored in 10 of 15 patients (67%). Nine of these patients were walking with assists within 2 weeks, including the one patient who had undergone bilateral prosthetic replacement. One patient, in whom ambulation was delayed until 12 weeks post surgery, had a concurrent pathological fracture of the humerus. The length of time that the patients were able to maintain their best postoperative ambulatory status (Table 2) was determined by the progression of their malignancy. On average, the 10 patients who walked postoperatively were able to maintain their ambulatory status for 76% of their survival. Prosthetic failure did not influence ambulation, except in one case of unrecognized dislocation. Of the five patients who failed to ambulate postoperatively, two had suffered pathological fracture of the contralateral femur and two were neurologically impaired. The bedridden period preoperatively for these 5 patients who never walked postoperatively averaged 9 weeks, whereas those 8 patients with pathological fracture in whom ambulation was restored spent an average of less than 2 weeks in bed prior to surgery. The two patients with impending fractures, who were ambulatory preoperatively, remained ambulatory postoperatively.

Overall Success: The overall clinical result was considered satisfactory if the patient was alive, relatively pain free and walking at 3 months. Based on these criteria, 10 of the 15 patients (67%) were considered a success.

Complications: Two patients in the series, both with neurological impairment, suffered a prosthetic dislocation. One dislocation, in a patient with spinal cord compression, occurred early and was initially unrecognized. This prosthesis remained dislocated and painful. The other dislocation occurred in a patient 8 months

Table 1

Patient	Age	Sex	Tumour Type	Presentation	Overall success 3 mos. survival, walking, pain relief	Complications	Survival (mos)
1	66	M	Prostate	Pathological fracture with failure of lade plate and cement fixation	Yes	Abductor detachment	40
2	51	F	Breast	Pathological fracture	Yes	—	12
3	34	F	Breast	Pathological fracture	—	Prosthetic dislocation	6
4	68	M	Multiple Myeloma	Pathological fracture	Yes	Abductor detachment, Removal of Prosthesis (33 mos)	36
5	53	F	Breast	Pathological fracture	—	—	2
6	66	F	Breast	Pathological fracture with failure of Enders pins	—	—	4
7	62	F	Breast	Pathological fracture	Yes	Abductor detachment	14
8	71	M	Leio-myosarcoma	Impending fracture	Yes	—	10
9	62	M	Renal Cell	Pathological fracture with failure of blade plate and cement fixation	—	Abductor detachment	8
10	51	F	Renal Cell	Pathological fracture	Yes	Abductor detachment, Prosthetic dislocation (8 mos) Hip Infection (14 mos)	17
11	60	F	Renal Cell	Pathological fracture	Yes	—	8
12	70	M	Prostate	Impending fracture	Yes	—	12
13	68	F	Breast	Pathological fracture with failure of DHS fixation	Yes	—	3
14	70	F	Lung	Pathological fracture with (bilaterally within 6 weeks)	Yes	Abductor detachment	6
15	60	F	Breast	Pathological fracture with	—	—	3

postreplacement following multiple cordotomies for control of pelvic pain. Open reduction of the dislocation was carried out and was followed several months later by a deep wound infection.

One patient required removal of the prosthesis at approximately 3 years postreplacement because of a penetrating decubitus ulcer. Thus, two patients (13%) required further hip surgery.

Specific to the tumour prosthesis is the problem of reattachment of the hip abductors. In six of the eight hips (75%) in which the greater trochanter was reattached to the prosthesis, subsequent radiographs demonstrated loss of abductor fixation. Radiographic assessment of abductor fixation was not possible in those 4 hips in which the divided tendon of gluteus medius was reattached to the prosthesis. No dislocation occurred in the most recent 4 patients, in whom the abductor, periosteum and vastus lateralis were left intact.

Miscellaneous early complications included one pulmonary embolism and two deep venous thromboses, all of which responded to medical management. There were no major wound complications in the immediate post-op period in spite of 13 of 15 patients having received preoperative radiation therapy.

Fig. 1-A: Preoperatove radiograph showing previously embolized destructive lesion involving entire proximal femur associated with avulsion fraction of greater trochanter.

Fig. 1-B: Postoperative radiograph demonstrating replacement of proximal femur with tumour prosthesis. Patient was ambulatory at 2 week and walked with aid of walker 5 months post-op.

Discussion

Proximal femoral replacement, employing a tumour prosthesis, has been used to bridge large bony defects associated with neoplastic disease. Moore and Bohlman in 1943[16] described the use of a custom-made metal component to replace the proximal femur in a case of giant cell tumour. The substitution of the upper two-thirds of the femur with a polythene prosthesis was reported by Seddon & Scales in 1949 (17). Since then, replacement using a tumour prosthesis has been described by several authors for use in both primary and secondary tumours involving the proximal femur, as well as for revision of failed standard total hip arthroplasty.[1 3 7 9 10 13 15 18 19] Most of the series report on the use of the tumour prosthesis in primary malignancy, with few series devoted to its application in metastatic disease of the proximal femur.[1 9 10 15 18 19]

The use of the prosthesis in metastatic disease is indicated when standard methods of treatment cannot reinforce or replace the compromised segment of bone. This situation occurs infrequently as indicated by our series in which only 16 tumor prostheses have been utilized in a 10-year period. These patients represent a small fraction of the patients with pathological fractures treated in our centre. Thus, the use of a tumour prosthesis is dependent on the extent of the skeletal disease. Skeletal defects which extend distally to extensively involve the intertrochanteric and subtrochanteric areas preclude the use of conventional total hip replacement because suitable bone for prosthetic seating

Fig. 2-A: Radiograph showing DHS fixation of original femoral neck fracture. Note there is no evidence of metastatic involvement.

Fig. 2-B: Radiograph 4 months later demonstrating extensive metastatic involvement of proximal femur with loss of DHS fixation.

Fig. 2-C: Postoperative radiograph showing use of tumour prosthesis to replace proximal femur. Patient was ambulatory at 1 week post-op and was able to walk with aid of walker until shortly before death at 3 months.

is not available (Fig. 1). If bone destruction extends proximally into the femoral head, then fracture stabilization, even when supplemented with methylmethacrylate, will fail because the remaining bone is insufficient to support metallic fixation. In addition, failure of previous pathological fracture fixation will severely compromise the remaining bone stock in the femoral head, making further attempts at fracture stabilization impossible. (Fig. 2)

The decision to use this prosthesis was usually made preoperatively by careful assessment of the radiographs. On occasion, the decision was made intraoperatively when the extent of the disease was found to be greater than demonstrated on the radiograph.

Reconstitution of abductor function is the primary challenge of repair following proximal femoral replacement. Almost all series reporting the use of a tumour prosthesis include a section devoted to techniques of abductor fixation. These include circlage wire or screw fixation to reattach the greater trochanter to the prosthesis[9 10], suture of the gluteus medius to the prothesis[3 7 10 15 18 19] or to the iliotibial band[1 3 7 8 13] lateral transfer of the iliopsoas[8] and the use of a silastic rod to invoke an intense fibrotic reaction in the newly formed abductor complex[1].

Bosquet et al[1], whose series utilized the same prosthesis as this series, reported excellent postoperative abductor function following postoperative immobilization for 12 weeks in a hip spica cast. Postoperative immobilization is unacceptable when dealing with patients with metastatic disease, in whom one of the priorities in management is to restore early ambulation. However, in agreement with other authors, this series demonstrates that early mobilization severely compromises the fixation of the abductors to the prosthesis. Six of the eight hips (75%), in which the greater trochanter was attached to the prosthesis, avulsed the bone fragment. Those cases involving soft tissue repair to the prosthesis or iliotibial band would be expected to have a similar outcome.

In response to this problem, the surgical approaches described by McFarland and Osborne[14] and modified by Hardinge[4] for exposure of the proximal femur and hip have been adopted for use in the last 4 patients. These approaches are based on the observation by these authors that the gluteus medius and vastus lateralis are in functional continuity through the thick tendinous periosteum covering the greater trochanter. The adaptation of the above approaches, described in earlier detail, permits ample exposure of the proximal femur while preserving the continuity of the gluteus medius and vastus lateralis. Following prosthetic replacement, the intervening tendinous periosteum is fixed to the prosthesis using the two screws and plastic plate. Tensile forces generated by abductor contraction are transmitted through the intact periosteum to the vastus lateralis and not to a tenuous repair of a divided tendon. Thus, restoration of abductor power is secured, while permitting early mobilization of the patient.

Prosthetic dislocation is a complication found in all series reporting the results of proximal femoral replacement with a tumour prosthesis. This complication is undoubtedly due to the complete division of the joint capsule and detachment of the stabilizing hip muscles. The incidence of dislocation in this series (12.5%) is similar to that experienced by previous authors (8 - 33%).[1 8 9 10 13 15. 18 19] Prevention depends on accurate prosthetic orientation and proper postreplacement tissue tension. The dislocations in this series occurred in patients who were neurologically impaired. Patients who have preoperative neurological defects should be considered for other forms of management, and cordotomies should be avoided where possible, in patients with a prosthesis already in situ. In addition, the high incidence of tumour prosthesis dislocations is directly related to the adequacy of the abductor fixation. There was no dislocation in the four patients in whom the current surgical approach was utilized. It is felt that this approach will minimize the future incidence of prosthetic dislocations.

The aim of surgical treatment of pathological femoral fractures is to reduce pain, restore ambulation, and obviate the need for subsequent surgical intervention. This series demonstrates that the tumour prosthesis fulfills these aims in most cases. The result with regard to pain relief (93% improved) is gratifying. Ambulation was restored in 67% of patients, with prosthetic failure influencing the ability to ambulate in only one patient. The preoperative bedridden period of those who did not ambulate (average 9 weeks) and those who did (average 2 weeks) indicates that early surgical intervention is helpful in achieving postoperative ambulation. Two patients (13%) required further hip surgery. Tumour progression within the involved femur has not resulted in prosthetic loosening or fractures below the prosthesis. The use of the tumour prosthesis did not affect patient survival. The survival figures are comparable to those found in series in which either conventional fixation techniques or proximal femoral replacement was used for metastatic disease.[1,3,4,13,15,18,20] When properly applied, this prosthesis will provide sufficient femoral reinforcement to last for the limited life span of these patients.

Conclusion

1. In patients with extensive metastatic disease of the proximal femur, in whom conventional forms of fixation are inadequate or have failed, a tumour prosthesis will prosthesis will provide excellent results with respect to pain relief and satisfactory results with regard to ambulation, depending on the extent of the disease.

2. Centres treating metastatic disease should have a tumour prosthesis available, as the decision to use it is occasionally made intraoperatively.

3. Early surgical intervention is necessary to restore ambulation.

4. The problem of fixation of the abductor mechanism to the prosthesis may be overcome by retaining its functional continuity, thus improving postoperative function and minimizing the risk of prosthetic dislocation.

Acknowledgements

I would like to thank Dr. R.J. McBroom, Dr. I. Macnab, and Dr. J. Dooley of the Division of Orthopaedic Surgery, Wellesley Hospital, for their assistance and supervision in the researching and preparation of this manuscript.

SPECIAL PURCHASE: PRICE REDUCED FROM $28.00 TO $14.00

THE CLINICAL CORE OF RESPIRATORY MEDICINE

BY DR. C. R. WOOLF

Professor of Medicine, University of Toronto, and Director of Respiratory Service, Toronto General Hospital.

A core information guide for medical students and residents as well as physicians in clinical practice. The full spectrum of lung disease is covered in 26 well-organized chapters. "Despite its small size, the book contains a tremendous wealth of information. . . The text is written in easy-flowing simple and delightful English. This book certainly deserves high marks". *Mayo Clinic Proceedings*

Copies available from Dr. C. R. Woolf Toronto General Hospital, Eaton Building, 10th Floor, Room 220 or Fitzgerald Building (South of MSB), Main Floor, Room 121

(Supply is limited at this reduced price)

References

1. Bosquet M., Burssens A., Mulier J.C.: Longterm Follow-up Results of a Femoral megaprosthesis. Arch. Orthop. Trauma. Surg. 97:299-304, 1980.
2. Dobbs H.S., Scales J.T. et al: Endoprosthetic replacement of the proximal femur and acetabulum. J. Bone Joint Surg. 63B:219-224, 1981.
3. Habermann E.T., Sachs R. et al: The Pathology and Treatment of Metastatic Disease of the Femur. Clin. Orthop. 169:70-82, 1982.
4. Hardinge, Kevin: The Direct Lateral Approach to the Hip. J. Bone Joint Surg, 64B:17-19. 1982.
5. Harrington K.D.: The Role of Surgery in the Management of Pathological Fractures. Ortho. Clinics of North America. 8(4):841-859, 1977.
6. Harrington K.D., Johnston J.O. et al: the Use of Methylmethacrylate as an Adjunct in the Internal Fixation of Malignant Neoplastic Fractures. J. Bone Joint Surg. 54A:1665-1676, 1972.
7. Harrington K.D., Sim F.H. et al: Methylmethacrylate as an Adjunct in Internal Fixation of Pathological Fractures. J. Bone Joint Surg. 58A:1047-54, 1976.
8. Jonsson R., Carlsson A. et al: Function Following Mega Total Hip Arthroplasty Compared With Conventional Total Hip Arthroplasty and Healthy Matched Controls. Clin. Orthop. 192:159-67, 1985.
9. Katzner M., Schringt E.: Etude de 100 Arthoplastics Totales de Hanche avec Megaprothese Femorale Realisees apres Resection Etendue de l'extremite Superieure du Femur. Int. Orthop. (SICOT) 6:233-242, 1982.
10. Knahr K., Kotz R. et al: Endoprosthesenimplantation Nach Resektion Maligner Extremitatengeschwulste. Z. Orthop. 117:967-973, 1979.
11. Lane J.M., Sculco T.P., Zolan S.: Treatment of Pathological Fractures of the Hip by Endoprosthetic Replacement. J. Bone Joint Surg, 62A:954-959, 1980.
12. Levy R.C., Sherry M.S., Siffert R.S.: Surgical Management of metastatic Disease of Bone at the Hip. Clin. Orthop. 169:62-69, 1982.
13. Lewis M.M., Chekofsky K.M.: Proximal Femur Replacement for Neoplastic disease. Clin, Orthop. 171:72-79, 1982.
14. McFarland B., Osborne G.: Approach to the Hip: a Suggested Improvement on Kocher's Method. J. Bone Joint Surg. 36B:364-7, 1954.
15. Meadeb P., Koechlin P., Apoil A.: Prosthese B.A.S.K. de Reconstruction apres Exerexe de l'extremite superieure du Femur pour Tumeur. Rev. Chir. Orthop. 67(7):655-8, 1981.
16. Moore A.T., Bohlman H.R.: Metal Hip Joint. A Case Report. J. Bone Joint Surg. 25A:688, 1943.
17. Seddon H.T., Scales J.T.: A polyethylene Substitute for the Upper Two-Thirds of the Shaft of the Femur. Lancet 2:795, 1949.
18. Wunderlich T., Blumlein H., Steeger D.: Die Tumorprothese zur Behandlung von Metastasen, Brothesenlockerungen und Frakturen am proximalen Femur. Z. orthop. 118:61-65, 1980.
19. Zichner l., Heiperta W.: Der Ersatz des proximalen Femurendes. Z. Orthop. 119:102-110, 1981.
20. Zickel R.E., Mouradian W.H.: Intramedullary Fixation of Pathological Fractures and Lesions of the Subtrochanteric Region of the Femur. J. Bone Joint Surg. 58A:1061-66, 1976.ric Region of the Femur.

The Nature Of Immunogenic Cells Within Bone Marrow

O.A. Karbi, 8T6
T.S. Axelrod, B. Fernandes, A.A. Czitrom

Introduction

The study of cytotoxic T-cell immune responses bears significant implication in tumour, reconstructive, and transplantation surgery. The precise identification of cells responsible for the induction of tissue immune responses is a prerequisite for future attempts at controlling the body's immune system.

In recent years purification methods for both responder and stimulator cells have greatly improved. It is now possible to study the alloreactive T-cells in vitro. It has been known for some time that T-lymphocytes recognize specific antigens, and the stimulator potential of various accessory cells has been analyzed. Recent work has stressed the importance of non-T, non-B, dendritic cells and macrophages as stimulators in primary mixed leukocyte reactions (MLR). However, it is now suspected that additional accessory cell types are capable of stimulating cytotoxic T-cells in vitro. We will attempt to show in this report that myeloid precursor cells (early granulocytes) are capable of stimulatory activity to the same extent as dendritic cells and macrophages. We will characterize these cells by density, adherence to glass, and the presence or absence of FcR and Ia antigens.

Abbreviations: Con A, concanavalin A; CTL, cytotoxic T lymphocytes; EDTA, ethylenediamine tetra-acetic acid; FcR, Fc receptor; NAd cells, non-adherent cells; Th cells, T-helper cells; Tc cells, T-cytotoxic cells; MHC, major histocompatibility complex; NDE, nonspecific esterase; MLC, mixed leukocyte culture; BSA, bovine serum albumin; Ts cells, T-supressor cells; EA, erythrocyte antibody; SRBC, sheep red blood cells.

Materials and Methods

Mice

Strains DBA2/J, C57BL/6J and C3H/HeJ were purchased from Jackson Laboratories, Bar Harbor, Maine. All of the mice used were females. DBA2/J were used as stimulators and C57BL/6J as responders in MLC's. The strains differ in their MHC and their haplotypes are H-2d and H-2b respectively. C3H/HeJ were used as stimulators and C57BL/6J as responders in some of the experiments. Their haplotypes are H-2k and H-2b respectively.

MLC and Generation of CTL

MLC was set up in round-bottom microculture plates with 0.1 ml each of responders and stimulators, in three concentrations of 1:1, 1:10 and 1:100 of responders to stimulators, and incubated at 37°C, 5% CO_2 for five days.

The stimulators were obtained by flushing out marrow from the pelvis, femur and tibia of DBA2/J female mice and layering them on gradients of 29%, 26%, 23% and 10% BSA and spinning at 14,000 rpm for thirty minutes. The responders were obtained from the spleens of C57BL/6J female mice. The spleens were homogenized and the suspensions enriched for T-cells by incubation at 37°C, 5% CO_2 for 45 minutes on a nylon wool column in 20% FCS (1).

The responder T-cells were then eluted with 20% FCS. Depletion of dendritic cells (2) and macrophages was carried out in some experiments on Sephadex 610 columns (1).

The stimulators were irradiated 2,000 R in order to prevent them from responding against the responder T-cells (3). At the end of incubation the effector cell population was assayed for cytotoxicity against 51Cr radio-labelled H-2d targets grown as a P815 tumour cell line in DBa-2/J mice (4). The effector CTL were incubated with the target cells for four hours, lysing the targets and releasing 51Cr into the medium. Released 51Cr was thus a measure of cytotoxicity and was measured on a gammacounter. The plates were set up with five concentrations of 1:1, 1:3, 1:9, 1:27 and 1:81 of targets to effectors. Each experimental well was set up in duplicate and the measure of radioactivity averaged between the two. The amount of 51Cr released was measured as % SPECIFIC 51Cr RELEASE and calculated as follows:

$$\frac{\text{Experimental value} - \text{Spontaneous release} \times 100}{\text{Mamimum release} - \text{Spontaneous release}}$$

where the value for SPONT. RELEASE was the average of three control wells with targets and medium where no lysis occured and the value for MAX. RELEASE was the average of three control wells with targets and hydrochloric acid where complete lysis occured. Cytotoxicity was also measured in LYTIC UNITS (5), a relative scale where 1 L.U. = 40% 51Cr

RELEASE, in order to compare the cytotoxicity of effector cell populations cultured with different stimulator bone marrow cell types.

Characterization by Adherence to Glass

The low-density cells of the A layer of bone marrow (which by morphology were mostly early granulocytes) were incubated on glass Petrie dishes at 37°C and 5% CO_2 in medium with 5% FCS. At the end of 2 hours, the non-adherent cells were washed off with medium and the 2-hour Ad cells were washed off with 3 mM EDTA (1). The 2-hour Ad cells were further incubated for 18 hours at 37°C and 5% CO_2 and were than separated into 18-hour Ad and NAd cells as previously described (1,3).

Characterization by Fc Receptor

10% EA mixture is prepared by incubating 1 ml of SRBC with 10 ul of 7SIgG anti-SRBC antibody for 1 hour at 37°C and 5% CO_2. "A" layer cells were rosetted with 10% Ea by incubating for 1 hour at 37°C and 5% CO_2. The mixture was then spun on Ficoll Hypaque at 3,000 rpm for 10 minutes so that A layer FcR+ cells would be in the pellet, and A layer FcR-cells would form a layer at the interface. SRBC were lysed in TRIS acetate buffer at 37°C (1,3).

Characterization of surface Ia antigens (6)

Stimulator cells were obtained by separating bone marrow of C3H/HEJ female mice (H-2k haplotype). 40 ul of anti-Iak was added to a 2 cc suspension of stimulator cells and incubated for 30 minutes at 37°C and 5% CO_2. The suspension was then pelletted and resuspended in rabbit complement (2 ml of 1:18 dilution) and incubated for 45 minutes at 37°C and 5% CO_2. The responder T-cells of the H-2b haplotype (C57BL/6J) were combined for a five-day incubation with H-2K A layer + Iak + complement and then assayed on Con A blasts derived from C3H/HEJ spleens. Controls were "A" layer cells alone and A layer + complement without antibody. Anti-Iak antibody activity was first tested against C3H/HeJ spleen-derived B-cells stimulated with LPS for 48 hours.

RESULTS

Bone marrow stimulator cells were found mostly in the A layer after BSA fractionation. They were found capable of inducing specific activation of CTL directed at H-2 alloantigens. Figure 1 shows that the peak of allostimulatory activity was best paralleled by a peak in the absolute numbers of myeloid precursor cells (early granulocytes). Other cell types did not show as good a correlation with the L.U. plot (Fig. 1).

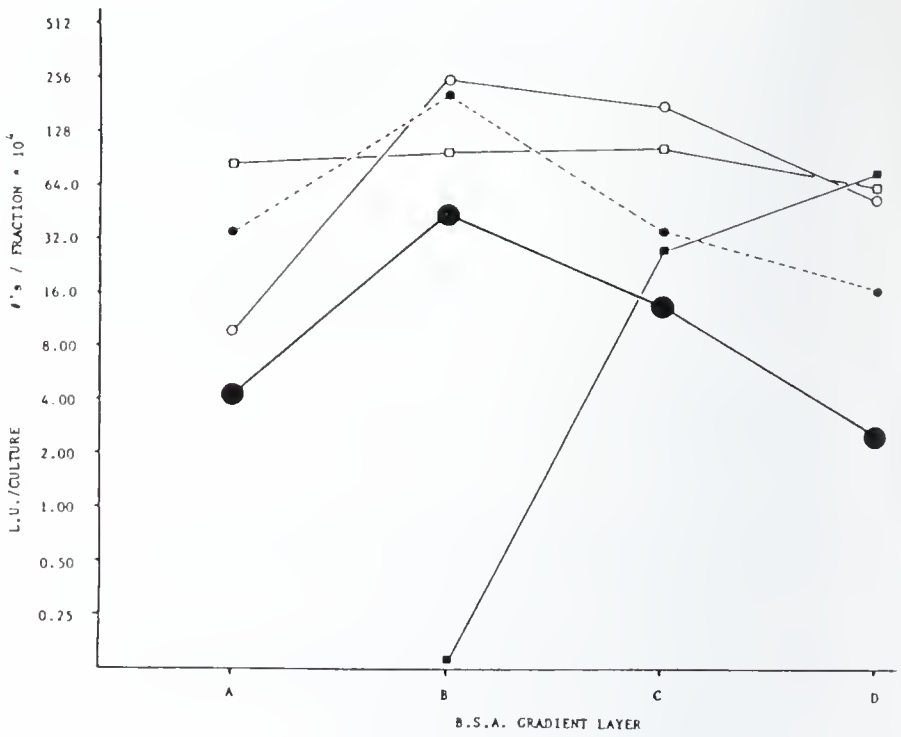


Fig. 1: ● L.U. Erythroid Precusors
○ Mature Granulocytes
■ Macrophages ●Early Granulocytes

At a given cell number, the comparison of lytic unit activity and morphology again showed that the enrichment profile for stimulatory activity paralleled the enrichment for the myeloid precursor cells:

Table 1

STIMULATOR	LYTIC UNITS/ CULTURE	MORPHOLOGY (%) EARLY GRANULOCYTES	MATURE GRANULOCYTES	LYMPH	ERYTH. PRECURSORS
A LAYER	4.0	46	4	0	48
B LAYER	2.5	24	69	1	6
C LAYER	< 0.6	10	35	38	14
D LAYER	< 0.6	0	8	65	26

* 40% ^{51}Cr Release = 1 L.U.

Characterization by adherence properties demonstrated that these low density cells from bone marrow (early granulocytes) become adherent to glass after two hours of incubation and non-adherent to glass after 18 hours of incubation:

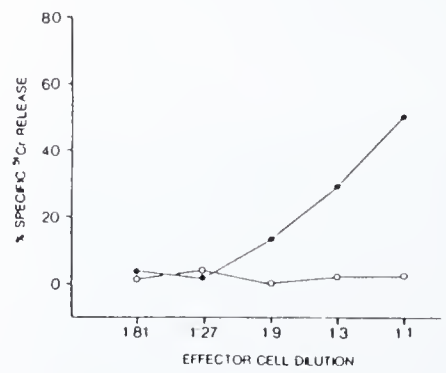


Fig. 2: ● 2-hr Ad
○ 2-hr NAd

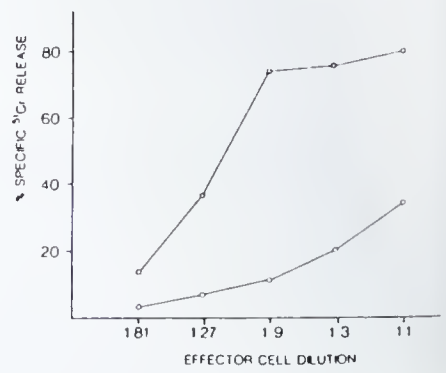


Fig. 3: ○ 18-hr Ad
□ 18-hr NAd

Characterization based on the presence or absence of the Fc receptor has shown that these early granulocytes lack the Fc receptor (they are FcR-) (Fig. 4). To rule out the possibility of phagocytosis of the SRBC by macrophages, subsequent death of the macrophages and hence the elimination of the FcR+ cells, thus making it seem that FcR- cells were the stimulatory ones, Fc-rosetting was also repeated with an incubation at 4°C —a temperature at which it is well known macrophages do not phagocytose — and the results were identical: FcR-cells showed substantially more allostimulatory activity than FcR+.

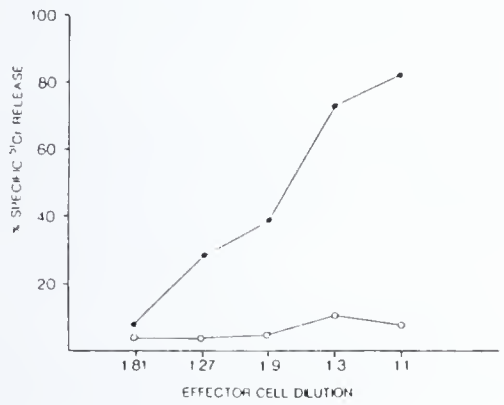


Fig.4: ● FcR- ○ FcR+

Fc rosetting and adherence experiments were combined into one on two occasions where the 18-hour Ad and NAd A layer cells were further differentiated into FcR+ and FcR- cells, thus resulting in four cell types which were cultured with C57BL/6J responders and the cultures assayed five days later. Out of the four groups the 18-hr Nad, FcR- cells were more stimulatory than the other three groups (18-hr Nad, FcR+; 18-hr Ad, FcR-; 18-hr Ad, FcR+) by a factor of five, with the other groups all showing consistently low % SPECIFIC 51 Cr RELEASE counts for all effector cell dilution (data not shown).

Characterization based on the presence or absence Ia antigen has shown that the stimulatory cells are Ia-negative. This experiment yielded higher % SPECIFIC 51 Cr RELEASE counts for bone marrow A layer cells treated with with anti-Iak and complement than for A layer cells alone or with complement, thus showing that the stimulatory cells lacked the Ia antigen because they survived the lysis of Iak cells by anti-Iak. Anti-Iak activity was substantiated by performing Iak lysis of spleen derived A layer cells of the H-2k haplotype in parallel with the above experiment. Spleen A layer cells being rich in Ia antigens, can be killed by anti-Iak and complement treatment, in their ability to stimulate CTL (1). In this experiment, spleen-derived A layer cells were effectively killed whereas bone-marrow-derived A layer cells were not, thus effectively demonstrating that our stimulatory cells are Ia- (data not shown).

The activity of the early granulocytes as CTL stimulators is equivalent to that of spleen derived macrophages and dendritic cells which are known stimulators of allogeneic T-cell responses.

Table 2

	LYTIC UNITS/ CULTURE	LYTIC UNITS/ 10^6 CELLS
BONE MARROW CELL (A LAYER, 2 HR AD. - 60% PMN PRECURSORS)	40.0	106.6
DENDRITIC CELLS	50.0	98.0
MACROPHAGES	59.0	176.1

Discussion

The principal finding of this study is the identificaton of the low density, early granulocyte, precursor cell as an accessory cell in cytotoxic T-lymphocyte responses. Previous studies have identified the non-T, non-B dendritic cells and macrophages as having the immunogenic potential to act as accessory cells. The precise mechanism of recognition, processing, and presentation of foreign antigens to CTL is not yet understood. However, the recognition of the heterogeneity in the accessory cell population has been held to support the speculation that different accessory cells might differentially activate distinct T-cell subsets in allogeneic responses, the subsets being T-helper lymphocytes. Our study refutes this concept. We have been able to demonstrate that the early granulocyte can mount strong allospecific responses by interaction with CTL. It is now understood that whereas helper T cells must *see* the alloantigen on the accessory cells, these accessory cells might be able to interact directly with CTL. This realization is relevant to the allograft response in vivo. Selective removal of allogeneic accessory cells from graft issue may well enhance our attempts at controlling the immune response. This has significationimmediate implications in tumour, transplant, and reconstructive surgery. This report characterizes the early granulocyte with respect to its glass-adherence properties, as well as lacking FcR and Ia receptors. Further studies are necessary to identify precisely the types of accessory cells and their respective roles in the immune response.

(Cont. on page 30)

Cyto-Pathology Associates

Consultation in Exfoliative Cytology

123 Edward St.
Toronto, Ont., M5G 1E7
Tel: 597-0539

Dr. A.E. Gray
Dr. R.C. Ross
Dr. D.W. Thompson
Dr. H.T. Van Patter

The Separation Of The Siamese Twins From Trinidad

M. E. Hoefert

Introduction

The conjoined twins Chang and Eng Bunker were born in Siam in 1811. They lived unseparated until their death at age 63. They did, however, lead full lives, fathering approximately 20 children between them. Through their exhibition by P. T. Barnum they became known as the Siamese Twins. Subsequently, this term has been used to describe all conjoined twins.

Conjoined twins develop when a fertilized egg begins to separate but does not split completely. The etiology is unclear but both maternal and environmental factors have been implicated. Although their approximate incidence is 1/50,000, the majority of conjoined twins are stillborn or die shortly after birth.[1]

The classification 2 of conjoined twins is based on their most prominently shared anatomical part:

thoracopagus — the chest wall
xiphopagus or omphalopagus — xiphoid or upper abdominal wall
pyopagus — back to back
ischiopagus — pelvis: side to side or end to end
craniopagus — head to head

Case History

In January 1985, two conjoined babies were born at the Port of Spain General Hospital in Trinidad. They were delivered by Caesarian section. Joined along the abdominal wall with pelves fused into a single ring, they were classified as omphalo-ischiopagus. (Fig. 1)

Shared structures included a bridge of liver, a colon, a common cloacus and a fused penis. The single colon and the two urethras emptied into the common cloacus. Both urethras and both corpora cavernosa were shared in the single penis.

The twins had separate chest cavities with independent hearts and lungs and separate spinal columns and cords. Each gastrointestinal tract had an individual biliary tract, pancreas, stomach, and small intestine, at which point they became fused into a single colon. Each twin had two kidneys-although one from each twin had been exchanged and was found in the opposite twin. Both twins had two ureters, a bladder, a prostate and two testes; neither had an anus. Each twin also had two functioning lower extremities.

Pre-Separation

Shortly after their birth the Hospital for Sick Children (HSC) in Toronto was contacted and within several hours had become involved.

Since the twins had been born without an anus, it became an urgent matter to perform a colostomy, and within two days of birth they were flown to Toronto.

Fig. 1 Twins prior to separation

(Jan. '85). Here, a loop colostomy draining both babies was performed through the original umbilicus. (Fig. 3). Pyeloplasty was also done since ureteral reflux was leading to a hydronephrotic kidney.

Having decided that a separation was indeed possible, Dr. Filler, Chief Surgeon at HSC, and Dr. Zuker, a plastic surgeon at HSC, flew to Trinidad in August of 1985. There they inserted seven tissue expanders into the twins. These would be progressively filled with saline over a six week period so that the expanded skin would aid in closing the massive tissue defect that would result following separation.

While many investigations may have been undertaken to assess the shared structures, only the minimum necessary were performed so as not to increase an already stressful situation for the twins.

Arteriography was not performed but the radiologists estimated that there was a 10-15% shared blood supply. CT scans proved the most helpful to determine what the twins shared.

Separation

The actual operation was performed by a 70-member team and lasted 22½ hours.

The main problems anticipated were technical problems associated with the anaesthesia and closure of the wound. The following are accounts of the work of the various specialties involved in the separation.

Anaesthesia

The main concerns here were fluid and blood volume, blood coagulation, blood chemistry, adrenal insufficiency and body temperature. Extensive monitoring was obviously required.

While the twins were not premedicated, they were given IV hydrocortisone prior to induction. As it is not uncommon for omphalopagus twins to lack an adrenal gland, leading to a sudden cardiovascular collapse, hydrocortisone was administered as a means of preventing possible adrenal insufficiency.[1]

They were pre-oxygenated and then simultaneously induced with thiopentone, atropine, and succinylcholine, followed by nasotracheal intubation. Maintenance was with N_2O_2, isoflurone, continuous morphine infusion, and pancuronium for muscle relaxation as necessary (determined by nerve stimulation). They also each had a CVP line, arterial B.P. monitoring, esophageal stethoscope, temperature probe, SaO_2 (transcutaneous determination of O_2 saturation) probe, EKG, and precordial stethoscope.

While the two anaesthetic teams worked closely throughout the operation, each child was looked after as a separate individual.

There were some problems with tissue expanders which limited diaphragmatic movement and caused increased bleeding from the blood supply of the capsules which had formed around them. Total blood replacement in Twin A was 14 times his original volume and 8 times in Twin B.

Plastic Surgery

Since there would not be enough skin left after the separation, the main problem here was how the wounds would be closed. As a result ingenious skin flaps were designed to help solve the problem. (Fig. 4) So that the lines marking the flaps would not be erased by the prep solutions, they were marked using surgical staples. There would still not have been enough skin to close the defects were it not for the tissue expanders. These were balloons implanted surgically in a subcutaneous position and progressively filled with saline. Dr. Rooparie Lalla, a plastic surgeon in Trinidad, was responsible for injecting saline into the tissue expanders over a six week period to achieve the total volumes listed Table 1.

Table 1: Total Volumes Achieved in Tissue Expanders

Tissue Expanders	Total Volume (mL)
2 intra-abdominal	1000 each
1 on each twin's chest	680 each
1 on Twin A's buttock	500
1 on each twin's R thigh	180 each

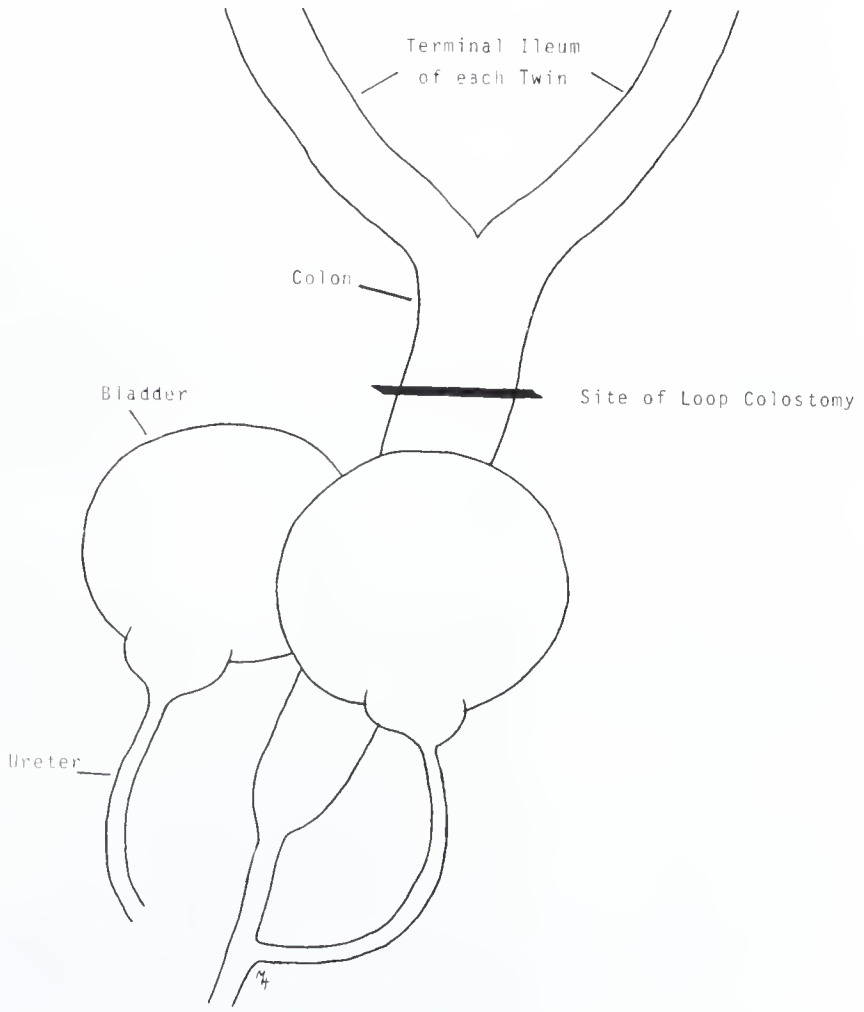


Fig. 3 Loop colostomy brought out through original umbilicus.

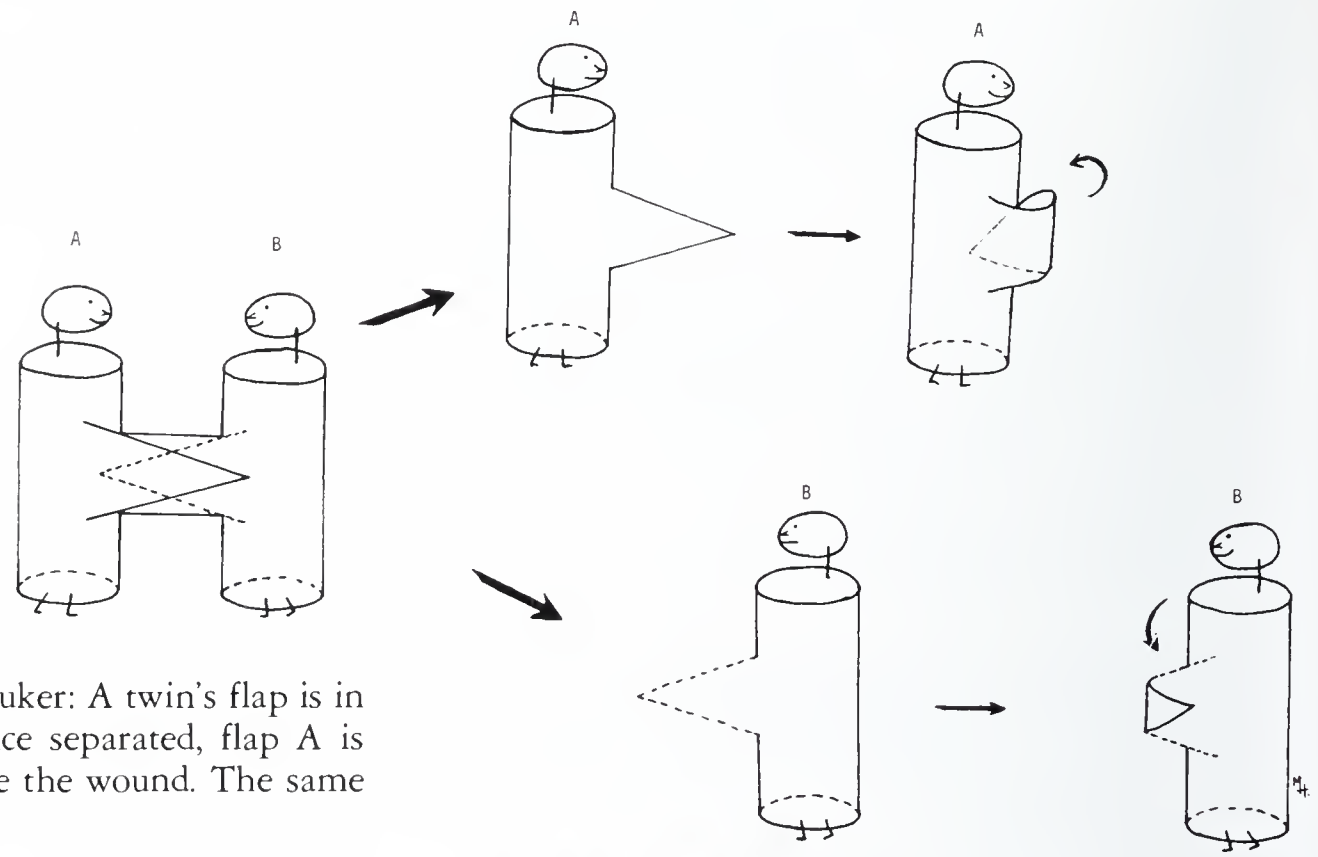


Fig. 4 Flaps designed by Dr. Zuker: A twin's flap is in front, B twin's is behind. Once separated, flap A is wound around twin A to close the wound. The same occurs with B's flap.

General Surgery

Once the abdomen was opened, the two livers — joined by a bridge of tissue — were separated first. The blood vessels were tied off and the bridge was then cut.

While each twin had his own small intestine they shared a single colon. The original colostomy loop was converted to a terminal colostomy for one twin. The distal ileum of the other was anastomosed to the distal part of the original colostomy loop. The terminal segment of the original colon hence became part of the terminal colostomy of the second twin. (Fig. 5)

Urology

While the twins had four kidneys altogether, one kidney from each twin had been exchanged and was situated in the opposite twin. The ureters were reattached so that they emptied into their respective bladders.

Both twins used Twin A's urethra pre-operatively although they each had their own (Fig. 6) The two urethras and the two corpora cavernosa in the shared penis allowed the construction of two penises and enabled both twins to remain as boys. Both twins have had erections since surgery and it is hoped that both will be continent.

Towards the end of the operation with time becoming an issue, it was decided to re-establish priorities and descend only one testis in each twin.

Orthopedic Surgery

The twins each had a complete pelvis but the two were fused into a single circle which forced the legs into abnormal positions. Due to the complex anatomical

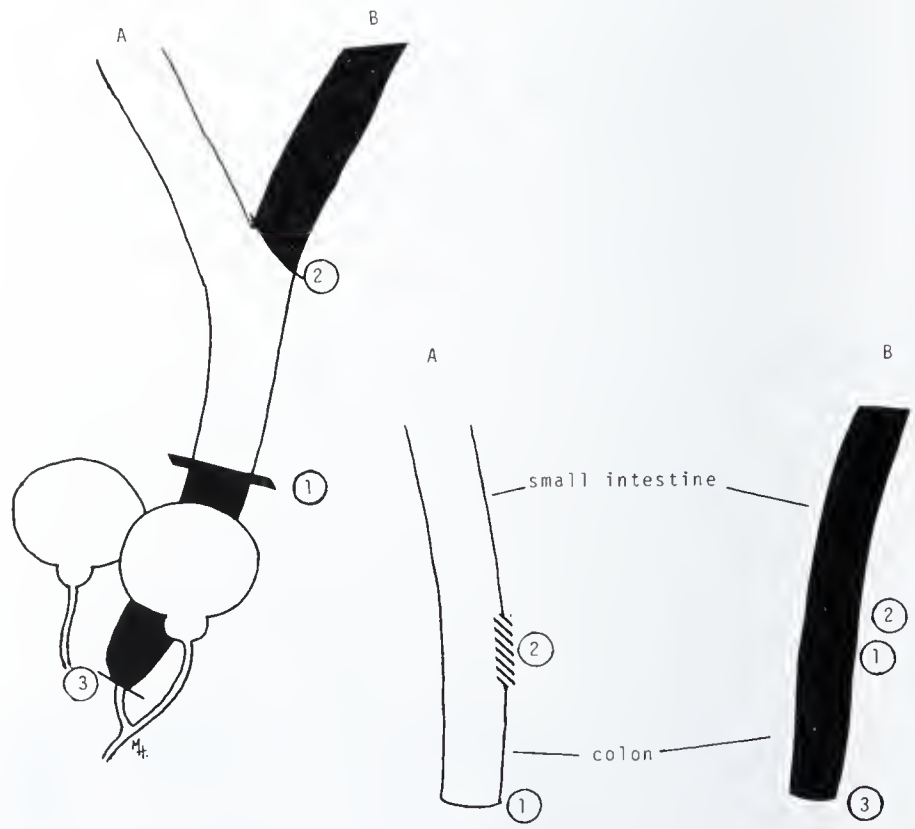


Fig. 5 i original loop colostomy and terminal colostomy of Twin A ii reanastomosed to i ending with iii — the terminal colostomy of Twin B.

arrangement CT scans were of little value here. After considerable discussion during the operation, the osteotomies were made as indicated in Fig. 7

Separation

The final cut that separated the twins was performed on Saturday October 26, 1985 at 11:21 p.m. A round of applause followed, after which two separate teams began to work on the twins.

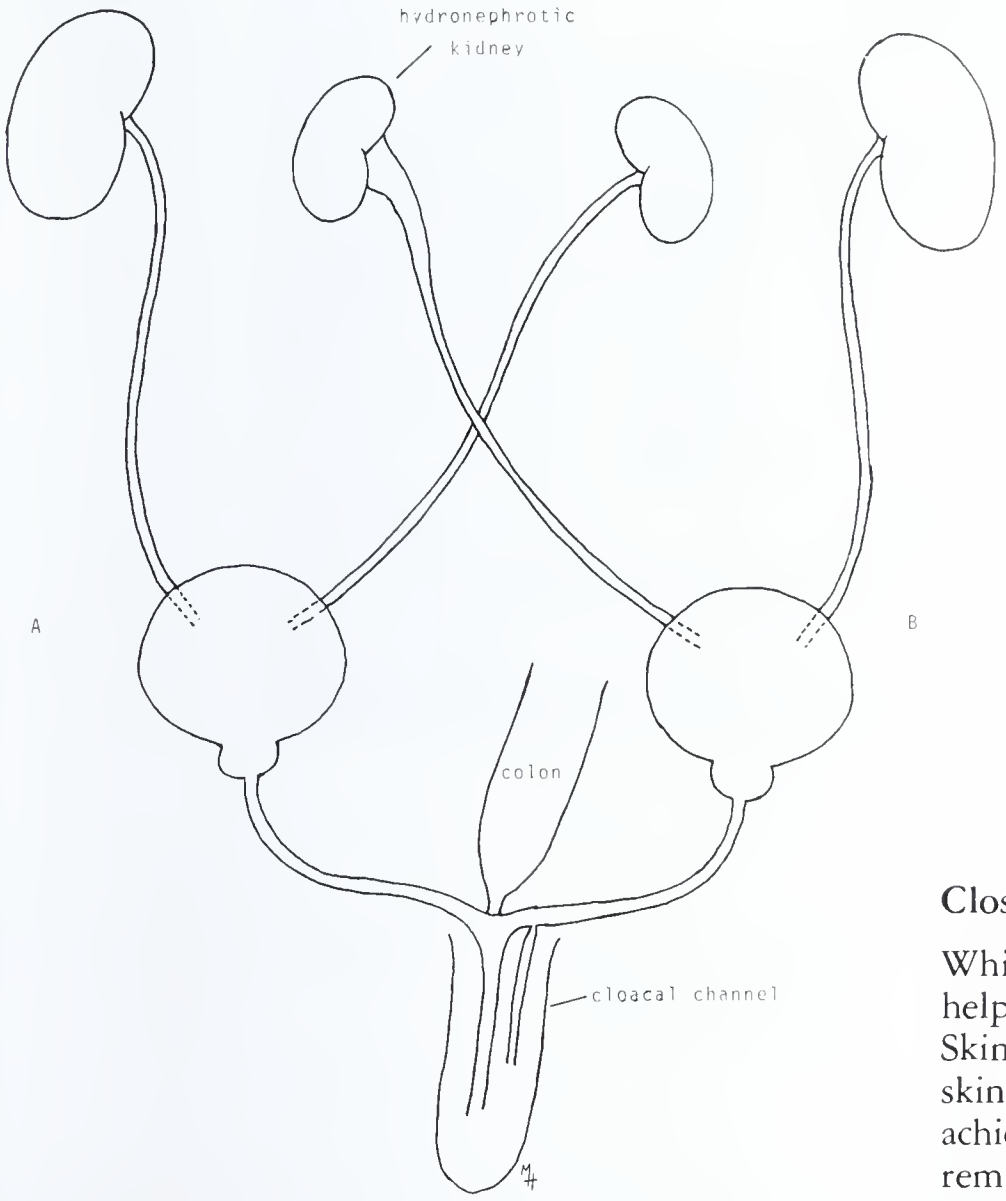


Fig. 6 Urological system prior to separation.

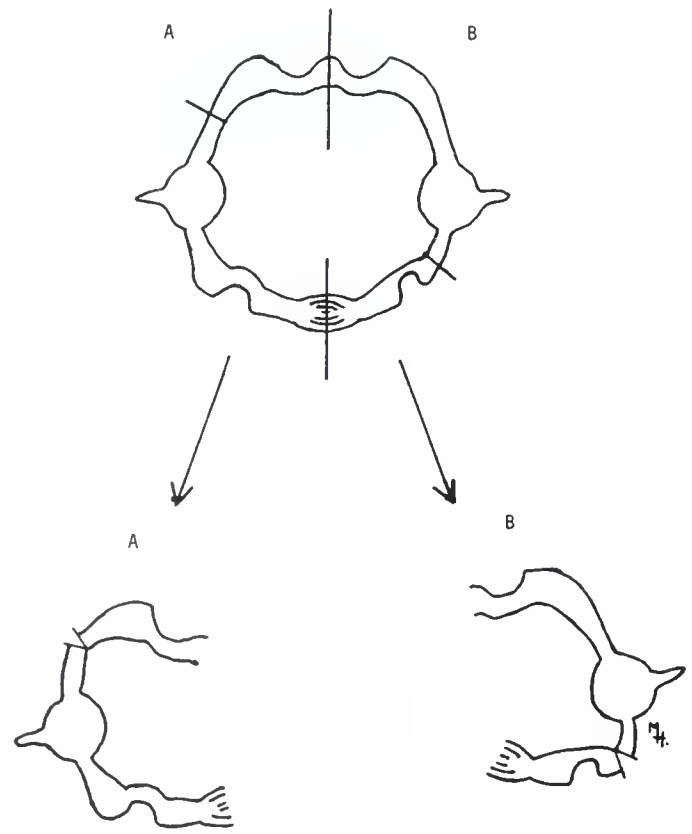


Fig. 7 Sites where osteotomies performed

Closure

While the stretched skin from the tissue expanders in helping closing the wound, it was still not sufficient. Skin closure on one twin's back was aided by the use of a skin graft. While good muscle approximation was achieved in closing the abdominal wall musculature, the remaining defect in one twin was closed using the capsule formed around an intra-abdominal tissue expander, while in the other twin a Marlex mesh was used.

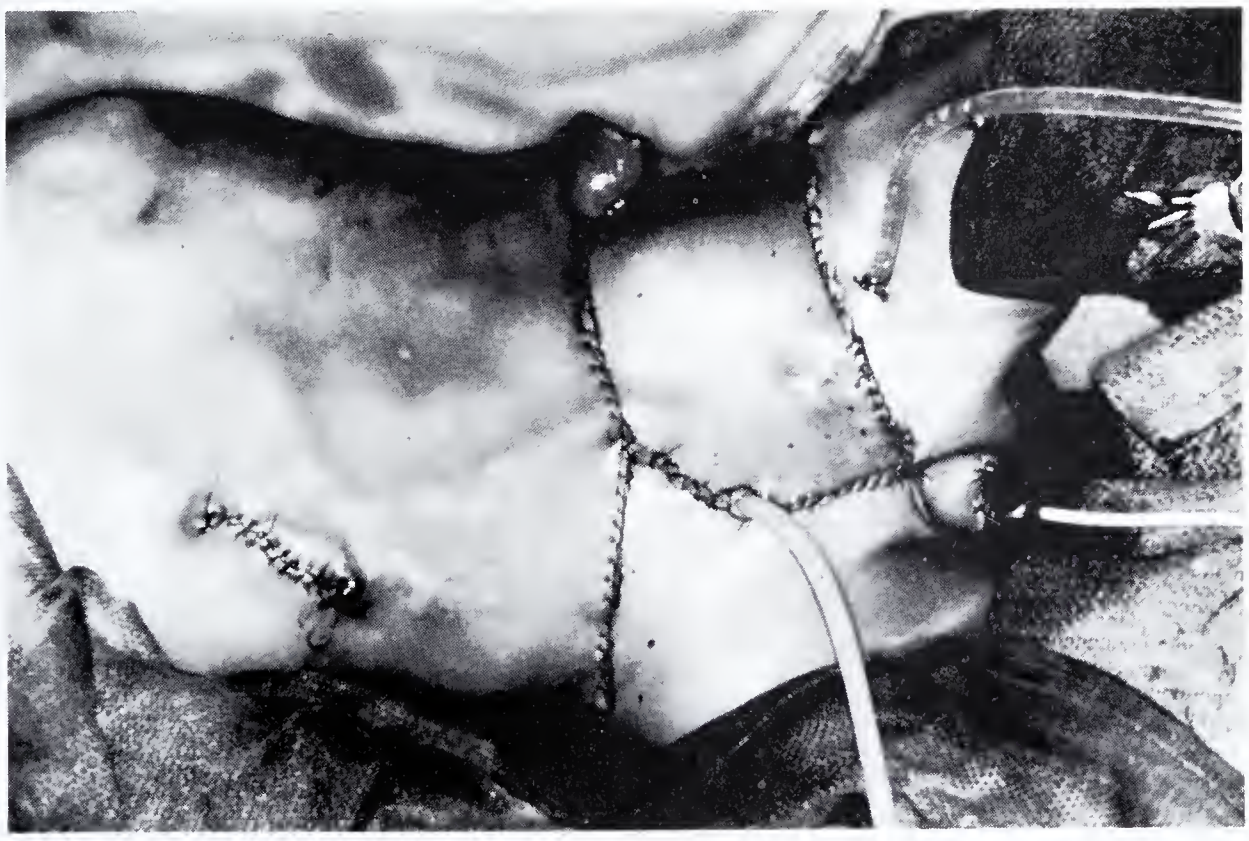


Fig. 7 Twin A post-separation.

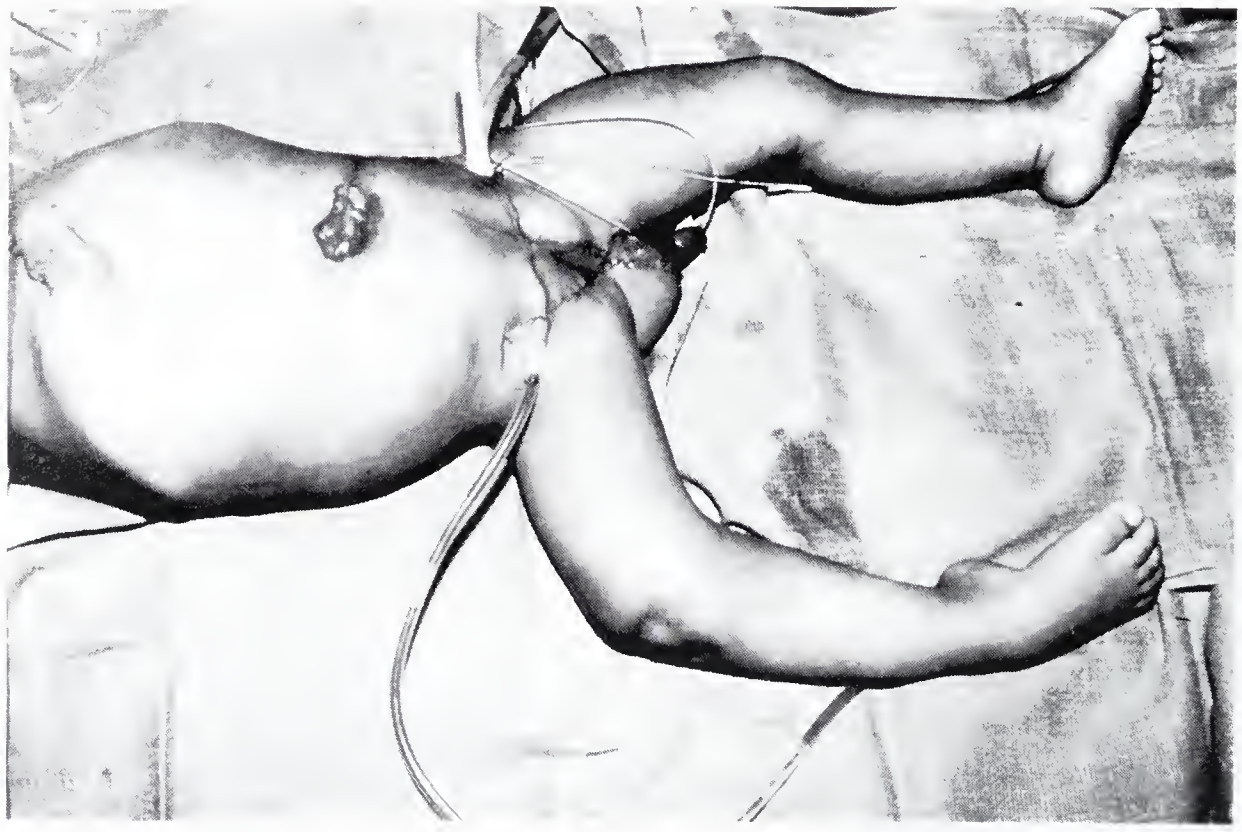


Fig. 8 Twin B post-separation.

Completion

The morning after, 22½ hours later, the twins had been separated and all incisions had finally been closed. (Fig. 8 & 9) They were then taken to the ICU and put in adjacent beds so they could see each other upon waking.

Summary

It is a rare occasion when so many specialties get together and successfully execute what can only be termed as an extremely rare and historical event.

As a result of the effort expended and the sophisticated technology available, these two twins can hope to live seemingly normal and separate lives.

Acknowledgements

I would like to express my gratitude to Dr. Zuker for giving me the opportunity to watch this operation and for his assistance in writing this article. Many thanks also go to Dr. Churchill for his help.

I would also like to thank Bruce Gray, Renée Hoops, Warren Mason, David Woods and Jane Ann Wyma for their help .

REFERENCES

1. James, P.D. McLeaod, M.E., et al. Anaesthetic considerations for separation of omphalo-ischiopagus tripus twins. Can Anaesth. Soc. J. 32 (4): 402, 1985.
2. Crocker, D., filler, R.M. Conjoined Twins. Ped. Surgery ed. 2 vol. 2. Year Book 1979.

(cont. from page 25)

REFERENCES

1. A.A. Czitrom, D.R. Katz and G. H. Sunshine. Alloreactive cytotoxic T-lymphocytes responses to H-2 products on purified accessory cells. Immunology, 1982, 45: 553.
2. Nussenzweig, M. and Steinman, R.M. J. Exp. Med., 1980, 151:1196.
3. G.H. Sunshine, D.R. Katz and A.A. Czitrom. Heterogeneity of MLR stimulator cells. Eur. J. Immunology, 1982, 12: 9-15.
4. A.A. Czitrom, et al. Stimulator Cell Requirements . . . Eur. J. Immunol., 1983, 130, 2: 546-550.
5. Cerrottini, J.C. et al. Generation of cytotoxic T lymphocytes in vitro. J. Exp. Med., 1974, 140: 703.
6. Yamashita, U. and Hamaoka, T. The requirement of Iapositive cells for the induction of hapten-reactive cytotoxic T lymphocytes in vitro. J. Immunol, 1979, 123: 2637.
7. Woodward, J.G., et al. Cell mediated immune responses. Requirement for an Iaâ macrophage. J. Immun., 1979, 122, 1196.
8. Steinman, R.M., and M.D. Witmer. Lymphoidd dendritic cells induce T-cell profileration. J. Exp. Med., 1976, 152: 1817.
9. Plate, J.M.D. and McKenzie, I.F.C. Nature New Biol., 1973, 245: 247.
10. A.A. Czitrom et al. Induction of Minor Alloantigen - sepcific T cell Subsets in vivo: Recognition of Processed Antigen by Helper but not by Cytotoxic T cell Precursors. J. Immun., 1984, 133; 1:33-39.

Respirology Rounds
Hyponatremia Associated with an Abnormal Chest Radiograph

Charles M. Price, M.D.
Robert H. Hyland, M.D., F.R.C.P.
Janet M. Roscoe, M.D., F.R.C.P.
Robin R. Gray, M.D., F.R.C.P.

A sixty-two year old woman presented to the emergency room of a peripheral hospital in April 1985, after having sustained a brief syncopal episode. Apart from mild hypertension there were no abnormal findings on physical examination. Serum biochemistry however disclosed a sodium of 124mmol/1, potassium 4.2 mmol/1, chloride 88 mmol/1 and total CO_2 of 28 mmol/1. Subsequent investigations performed over the next few weeks included a normal chest radiograph, normal brain scan and skull radiograph, a urinalysis which revealed 1+ albumin and a 24 hour creatinine clearance of 0.87 ml/sec (Normal 1.24-2.08). A resting EKG was normal, however a 24 hour Holter recording showed frequent ventricular extrasystoles. Diuretic therapy was instituted for her hypertension.

The patient was admitted to a tertiary care centre in September 1985 for further investigation of her hyponatremia. At this time she complained of a decrease in her appetite with an unquantified amount of weight loss over the previous three to four months. She was also bothered by an exacerbation of her chronic lumbar back pain, which had been attributed in the past to degenerative disc disease. She had been a 1-2 pack per day smoker for many years but denied cough, dyspnoea or hemoptysis. There were no changes in bowel habits noted, no neurologic complaints, no fever or sweats. Physical examination revealed an obese woman with a blood pressure of 190/90. Positive physical findings included dullness to percussion and decrease in breath sounds over the right anterior chest. There was sternal tenderness as well as pain in the lumbar spine on movement in all directions. Serum sodium was 129 mmol/1., potassium 3.6 mmol/1., chloride 90 mmol/1 and total CO_2 27 mmol/1. Her creatinine was 75 mmol/1. and blood urea nitrogen 4 mmol/1. Her chest x-ray is shown below.

What is your diagnosis?

BEST WISHES TO THE GRADUATES OF 86.

Alpha Laboratories Inc.

ANALYSIS AND RESEARCH IN
MEDICAL, PHARMACEUTICAL, FOOD AND COSMETICS

DR. C. JOSEPH KURIAN
449-2166

285 LESMILL ROAD
DON MILLS, ONTARIO

W.B. Saunders Company
Canada Limited
WORLD'S LARGEST
HEALTH SCIENCE PUBLISHERS
Distributors for: **Merck Inc., Praeger Scientific, Bailliere Tindall, Igaku-Shoin, Springhouse, Slack Inc.**
One Goldthorne Ave., Toronto, ON. M8Z 5T9
(416) 251-3787
Available through
U of T Medical Bookstore

The Spectrum Of Stroke: *A Case Report*

Robert Mounsey, Fred Parker
Stephen West, Elizabeth Whittle

Introduction

Atherosclerosis is the most common disease of Western society. This disease process presents a significant health problem, and thus receives much medical attention. Atherosclerosis is a general term delineating a variety of pathological conditions resulting from induced proliferation of smooth muscle cells in the walls of arteries. The World Health Organization defines atherosclerosis as, "a variable amount of changes of the intima of arteries consisting of focal accumulation of lipids, complex carbohydrates, blood products, fibrous tissue, calcium deposits and associated medical changes".[11] The two most serious consequences of atherosclerosis are myocardial infarction and stroke. We report a case of stroke in a 50 year old male, tracing the entire course of events from risk factors to postoperative occurrences.

Case Report

Six months prior to the current admission, this 50 year old man was admitted to hospital with an elevated blood pressure of 170/110. He was treated with 100 mg o.d. Atenolol (Tenormin).

On examination, no carotid bruits were heard, but a distinct bruit was audible over the left femoral artery. The remainder of the physical examination, including heart sounds, was normal. On learning of his past medical history, it was discovered that he had suffered a myocardial infarction ten years previously. He was retained in hospital for two weeks on the above medication and at the time of discharge, his blood pressure was constant at 140/70.

Four months later, the patient was again admitted to hospital with a five-day history of increasing left-sided arm and leg weakness and deterioration in concentration. On physical examination, an obvious left-sided facial droop and left hemiparesis was noted. Carotid angiography was performed and revealed a complete occlusion of the right internal carotid artery. A right carotid thromboendarterectomy was attempted immediately, but was unsuccessful in totally clearing the vessel to allow flow. The right internal carotid artery was subsequently ligated.

His final admission was due to a sudden onset of confusion and some right-handed weakness. Angiography was once again performed and showed a 60% stenosis at the left internal carotid artery at the siphon region that was not accessible by surgery. A right EC/IC (extra-cranial -intra-cranial) anastomosis was performed on the patient connecting the superficial temporal to the middle cerebral artery to restore flow to the right side of the brain. No complications were reported during surgery.

The patient regained consciousness and was found to be restless and confused for several days after the operation. He experienced pain on micturition, as well as experiencing difficulty in taking food by mouth. Four days after the operation the patient became comatose, and his respiration became very irregular. He was suctioned on several occasions to remove thick mucous that was accumulating in his airway. Two days later, his respirations ceased and he was pronounced dead.

Radiology

Before the thromboendarterectomy a CT scan was performed, with and without enhancement. Adjacent to the left caudate nucleus and in the corona radiata, tiny lacunes were seen; these were of questionable significance. More importantly, no hemorrhage was seen.

A second series of radiological tests were performed two days later. A repeat CT scan revealed a patchy area of decreased attenuation in the right posterior parietal region. There is no mass effect associated with this lesion. The previous CT scan failed to reveal this defect. As in the previous scan a small left lacunar infarct was noted.

In order to make a clear assessment of the state of the intra- and extra-cranial vessels, cerebral angiography was done in the second radiological series. The right femoral artery was chosen, and a catheter was passed in a retrograde fashion, enabling study of the right and left common carotid arteries. Anterior-Posterior (AP) and lateral projections of the intracranial and cervical portions of both vessels were studied. From this procedure it was determined that right internal carotid was totally occluded 1 cm from its origin. There was some reflux of contrast material into the distal internal carotid artery from a left carotid injection indicating complete occlusion of the right internal carotid artery, including the

cervical and petrous portions. The other arteries of the region (the right superficial temporal, right vertebral and basilar) were essentially normal. The left internal carotid appeared to be 60% stenosed in its proximal cavernous portion. Apart from a slight irregularity of the horizontal portion of the left middle cerebral artery the other vessels in the region were unremarkable.

Surgical Findings 1

The right carotid thromboendarterectomy was attempted on January 14th. An incision was made along the anterior border of the right sternomastoid muscle and the carotid vessels exposed. The bifurcation of the common carotid artery appeared normal but the internal carotid just distal to the bifurcation was bulbous and yellow. Immediately distal to this it was narrower and a bluish color, with no pulse. Vessel loops were placed around the carotid vessels and the common and external carotid arteries were occluded. An arteriotomy was produced in the internal and common carotids and a dark thrombus was observed in the internal carotid. The thrombus was carefully removed and a tail of bluish clot was withdrawn from the lumen of the vessel, but no reflux flow occurred from the distal internal carotid artery.

A Fogarty catheter was passed approximately 8 cm distally in the internal carotid artery, and several attempts were m ade to withdraw the clot. A small amount of dark clot was retrieved, but reflux flow could be obtained.

Therefore, the distal internal carotid artery was ligated with three clips. An endarterectomy was performed on the bifurcation of the common carotid artery, but there was little atheroma.

The origin of the external carotid artery was reconstructed to create a smooth passage from the common carotid to the external carotid, and the vessels were unclamped. The distal external carotid artery was seen to be pulsatile, and the would was then closed.

Postoperative Course 1

Following the attempted right carotid thromboendarterectomy, ligation of the right internal carotid artery, and right carotid bifurcation endarterectomy, the patient seemed to recover well. There was no recurrence of left facial nerve palsy nor left hemiparesis. Three days postoperatively, the patient's hypertension worsened, and he was restarted on Atenolol (B-adrenergic blocker), Nifedipine (Ca-channel blocker), and Hydralazine (vasodilator). The patient was discharged and arrangements were made for a six-week followup.

Radiology

Three months after the attempted thromboendarterectomy, the patient was again admitted to hospital because of left cerebral ischemia, and another series of radiological investigations were undertaken. This included CT scans and angiography, which showed the right internal carotid was still occluded. These studies enabled the surgeon to assess the state of the vessels and note where the right internal carotid was ligated in the previous thromboendarterectomy. This assessment was necessary to perform the next operation, an Extra-Cranial — Intra-Cranial anastomosis. This was done to try and alleviate the growing cerebral ischemia.

Surgical Findings 2

It was decided to perform an Extra-Cranial/Intra-Cranial (EC/IC) bypass around the occluded right internal carotid artery.

Under general anesthesia the patient's head was turned so that the right temporal region was in the horizontal plane. A C-shaped incision was made in the right temporofrontal region and the superficial temporal artery exposed. It divided into an anterior and posterior branch, and the posterior branch was chosen as the donor artery. It was dissected off with the aponeurosis and subcutaneous tissue attached.

A small craniotomy was then performed and the bone flap turned to expose the Sylvian Fissure. A branch of the middle cerebral artery which emerged from the Sylvian fissure over the frontal side about one inch anterior to the motorstrip was chosen as the recipient artery. Using a microscope, the artery was dissected from the surrounding arachnoid.

Then the adventitia of the donor artery was removed, and it was cut on an angle and clipped. The lumen of the artery was irrigated with heparinized saline. A piece of rubber was placed under the recipient artery and temporal clips attached on each side. An incision was made in the artery and the lumen irrigated. Anastomosis was performed using 10-0 nylon.

When the clips were removed, good flow was obtained from the donor to the recipient artery. The posterior portion of the divided temporalis muscle was placed over the brain to perform encephalomosynangiasis to increase blood supply to the brain. The dura was partially closed, and a small piece of the bone flap removed to make a passage for the donor artery. The bone was put back together with wire, and the scalp closed in layers.

Postoperative Course 2

Following postoperative recovery of the EC/IC anastomosis, the patient was unable to follow objects well and showed mild dysphasia. Two days postoperatively the patient had a hypertensive episode which was treated with Hydralazine; Expressive dysphasia was more pronounced and the patient could not understand requests. The patient showed signs of bilateral cerebral dysfunction and lapsed into coma. Decorticate postur-

ing (flexion of upper limbs and extension of lower limbs), indicative of left cerebral hemisphere stroke secondary to carotid artery occlusion was evident. The patient became comatose, had fixed pupils, and bradycardia.

By the fifth postoperative day, the patient was apneic, and upon suctioning, copious amounts of mucus were obtained. The patient's respiration soon ceased and he was pronounced dead.

Discussion

Stroke is a widespread disorder which afflicts 500,000 North Americans yearly, of whom 40% die within one month. Stroke constitutes the third most common cause of death in the Western world. Of the 60% who survive the initial event, 50% require long-term hospitalization and chronic care.

Therefore, recognition and preventative treatment of stroke candidates are needed if stroke incidence is to be avoided. Mentioned below are various factors which are known to have a positive correlation with stroke incidence. In the case of our 50-year-old man, several of these factors were present.

According to the Framingham Study by Wolf et al, the incidence of stroke is lower and occurs later than myocardial infarction. In fact, according to Wolf, "stroke incidence lagged that of MI by more than ten years".[1] It is interesting that our patient suffered a MI ten years previous to his onset of symptoms of stroke.

Various studies have shown that stroke incidence increases with the age of the patient, and that the incidence more than doubles with each successive decade beyond age 40.[1,2] In our case, the patient was 50 years old and hence his risk for stroke would have increased to some extent.

It has also been found that the incidence of stroke for men exceeds that for women, but that this parameter is not striking.[1]

One of the main predisposing risk factors for stroke evident in this patient was hypertension. Studies show that a diastolic blood pressure above 110 causes a 1.23—2.89 fold increase in the incidence of stroke.[2,3] This man, at the time of his first reported hospitalization, had a blood pressure reading of 170/110, and therefore, was at risk. Other studies also emphasize this.[1,4,5,6]

This patient, on his first reported hospitalization, exhibited a borderline left ventricular hypertrophy, which, according to the Framingham Study, increases the risk of stroke in men by five-fold.[1]

Persons with a history of coronary heart disease and cardiac failure have a much higher incidence of stroke than those without any such history.[1,4,6,3] As already noted, this patient had suffered a myocardial infarction ten years previously. It should also be noted that if a person possesses both coronary heart disease and hypertension, as did this patient, his risk of stroke is greater than the sum of the individual risks.[1]

Finally, much controversy has always surrounded the idea that cigarette smoking is a dominant factor leading to higher stroke incidence. Recent evidence by Rogers et al, has shown that smoking causes a reduction in the blood flow to the hemispheric gray matter. It has also been shown that a reduction in cerebral blood flow supplying the gray matter is associated with various types of cerebrovascular disorders, e.g. Transient Ischemic Attacks, and Reversible Ischemic Neurological Deficits and remote strokes.[7] Thus it would appear that this should increase the incidence of stroke. Other studies by Ball et al[8] have shown that continued smoking increases the risk of sustaining cerebral infarction by a factor of 1.9 for men and 2.4 for women. This was only determined for cerebral infarction. Smoking did not prove to be significant in the case of cerebral hemorrhage. In this case, the patient had been smoking one package of cigarettes per day for the past twenty years.

Several modes of treatment are currently available for the stroke patient. In the case presented, thromboendarterectomy was performed.

This procedure is indicated when the patient meets two criteria. First, he should demonstrate signs and relate symptoms of cerebrovascular insufficiency referable to the internal carotid artery below the base of the skull. Such symptoms include amaurosis fugax, central retinal artery occlusion, reversible ischemic neurological deficits (RIND's) (lasting more than 24 hours) and carotid distribution transient ischemic attacks (TIA's) (lasting less than 24 hours). It is worth noting that this patient experienced TIA's. The second criterion to be met is the demonstration of stenosis in the internal carotid artery by means of angiography. This patient exhibited marked stenosis in both the right and left internal carotid arteries.

Endarterectomy is contraindicated in patients who have suffered a recent myocardial infarction and are not well enough to withstand surgery.

At this time, there is a good deal of controversy surrounding the issue of whether to perform an endarterectomy on asymptomatic patients who possess only a carotid bruit. There have been a number of recent reports that surgical mortality and morbidity rates following the procedure may not justify the risks of surgical intervention.

Carotid endarterectomy is effective in relieving the symptoms of TIA's and in lowering the incidence of stroke in selected patients.[9,12,13] However, a number of complications may arise. The most common of these is embolism from ulcerated atherosclerotic material. This leads to postoperative neurological deficits. Thrombus formation may occur due to severe postoperative hypotension. If a patch graft is used, aneurysms occasionally occur. Myocardial infarction (MI) is a fairly common cause of the infrequent deaths during the operation. A

hematoma may occasionally occur anterolateral to the trachea and cause symptoms due to neck distention and tracheal compression.

A recent study by Sundt and his co-workers related the rate of mortality and serious morbidity following endarterectomy to preoperative risk factors.[10] The most significant finding was that neurologically stable patients without major medical and angiographically demonstrated risks incurred no mortality and had a 1.2% incidence of MI and a 0.6% incidence of minor stroke. Neurologically unstable patients (with or without major risks) suffered the highest rate of neurological complications following surgery, having 14.2% incidence of major stroke and a 2.1% incidence of minor stroke.

The carotid thromboendarterectomy that was attempted in this patient was not successful in removing the entire clot. The was due to the fact that the thrombus extended beyond the base of the skull into an area which the catheter could not reach.

EC/IC bypass was first performed in 1967 by Yarsagil and Donaghy, and is generally considered in cases where a lesion in a cerebral blood vessel is inoperable or inaccessible.[23] Twenty to thirty percent of all TIA victims are diagnosed as having such lesions.[17] Since patients experiencing TIA's have a 10-20% chance of experiencing a stroke within a year,[15 16] it is clearly important to restore blood flow to the affected area.

It is more effective to do small (as opposed to large) vessel anastomosis because the distribution of atherosclerosis is usually at the bifurcation of larger vessels. Lesions in larger vessels at the base of the brain can be bypassed in this manner.[23]

Following the procedure the donor artery may go into spasm. However, normal flow usually resumes quickly and the vessel will subsequently enlarge to three times its original size over several months.[22] Measurements of cerebral flow through these vessels have confirmed this by showing, on the average, an increase in blood flow through the artery form 20 — 60 ml/min.[15]

There are several criteria which a patient should meet before this procedure is attempted and these can be divided into clinical and radiological signs. Clinical symptoms include the presence of TIA's, RIND's, progressive stroke and completed mild stroke.[15 22] Radiological indications are occlusion of the internal carotid artery, lesions in a surgically inaccessible portion of the internal carotid, and stenosis or occlusion in the middle cerebral or basilar arteries when adequate collateral circulation is not present.[15 22] Note that this patient was suffering TIA's due to a complete occlusion of the right internal carotid artery and a severe stenosis of the left internal carotid artery in an inaccessible region.

Contraindications for an EC/IC bypass include severe static prolonged neurological deficit, advanced intracranial small vessel disease, cerebral ischemia in the acute edema stage, multiple vascular stenoses, scalp donor vessels which are less than 0.8 mm in diameter and cardiovascular or pulmonary disease.[14 22]

A number of complications may arise from this procedure. Scalp ischemia is a rare complication because of rich collateral circulation. Subdural hematomas and hygromas occasionally occur and the patient may be left with a permanent neurological deficit due to the occlusion of the recipient vessel during the operation.[22] Operative morality rates are low, between 2 and 3 percent.[22 23]

The success rates of an EC/IC bypass depend on the preoperative status of the patient. Eighty-five to ninety-five percent of patients suffering from TIA's or RIND's are improved or become completely asymptomatic.[14 15]

Patients suffering from progressive stroke exhibit a 60% improvement rate,[14] although other studies claim a higher figure.[23] Patients who have experienced a completed stroke, exhibit, on average, a 51% improvement rate[17] whereas, without the procedure, 30 — 40% of all patients who have suffered completed stroke would die from a second stroke within three years.[14]

The purpose of a bypass is mainly to reduce the incidence of TIA's and decrease the risk of stroke. In this class of patients, symptoms are usually due to insufficient blood supply as opposed to embolism. Therefore, the degree of neurological impairment is not related directly to major vessel lesions but to the paucity of collateral circulation. EC/IC bypass is an attempt to augment collateral circulation.[14 22 23]

Survival And Recurrence Factors

In the early stages following stroke (one to two weeks), the potential for rehabilitation may be evaluated in relation to the pathology and anatomical location of stroke. However, for long-term rehabilitation potential, other factors influence the outcome.

Gersten has found certain variables which are useful in the evaluation of stroke victim's potential for recovery.[18] The following factors were found to be good predictors of favourable prognosis: positive acceptance of the disability, the presence of a spouse at home, good bladder control, good visual motor coordination, early return of muscle tone, regained strength in hand and trunk muscles, and ability to feed oneself.

The most consistent negative predictors of stroke outcome were found to be the following: perceptual and/or cognitive dysfunction, prior stroke, delay in initiating therapy, the presence of nystagmus, and poor motivation.

In all modalities, the majority of recovery occurs within three months, after which, improvement does not reach statistical significance. However, Lehamann et al[19] has shown that rehabilitation therapy provided six months to a year following acute stroke may lead to a measurable improvement.

In the well-known Framingham Study[20] 5,209 men

and women were followed for 26 years for cardiovascular disease, including stroke. It was found that of the 394 strokes (7.6% of participants), the majority (57%) were atherothrombotic brain infarctions. The complete breakdown of stroke distribution was as follows:

TABLE 1. Distribution of Initial Stroke by Type, 26 Year Followup.[20]

	NUMBER OF CASES MEN	WOMEN	PERCENT OF ALL STROKES
Atherothrombotic brain infarction	111	111	57%
Cerebral embolus	30	33	16%
Intracerebral hemorrhage	10	7	4%
Subarachnoid hemorrhage	16	23	10%
Transient Ischemic Attack only	25	16	10%
Stroke from other causes	6	6	3%
	198	196	100%

With respect to survival rates, intracranial hemorrhage was found to account for the majority of the thirty-day fatalities. In mean, the presence of pre-stroke hypertension was well correlated with increased mortality. Age of stroke onset is also an important factor in survival. Long-term survival rates seem to be higher in women than men. The rates of stroke recurrence have been found to range from 13% to 53%.[21] Cardiovascular disease and hypertension were found to be major determinants of stroke recurrence.

Within the critical 30-day period following stroke, the major cause of death was seen to be the stroke itself. However, cardiovascular disease is the major cause of death among long-term survivors.

Treatment of hypertension and congestive heart failure is thought to be beneficial for long-term survival. However, over-zealous treatment of hypertension following stroke may further compromise cerebral blood flow. It is presently believed that the benefits of hypertensive treatment outweigh the potential hazards. Congestive heart failure and coronary heart disease are also contributing factors in stroke recurrence. Thus it is important to effectively treat these cardiac problems in addition to controlling hypertension to improve long-term survival, following stroke.

Conclusion

The case which is reported here illustrates many of the aspects of stroke management. The patient had several risk factors (hypertension, age, sex, smoking, borderline Left Ventricular Hypertophy and previous myocardial infarction). He presented to the attending physician with the classic symptoms of TIA's. A thromboendarterectomy was performed but was not successful in removing the thrombus. The patient's symptoms recurred and an EC/IC bypass was carried out. Following operation, the patient's condition deteriorated rapidly and six days following the operation, he died.

(Cont. on page 16 & 48)

Fig. 1 An arteriogram showing the major vessels of the aortic arch.

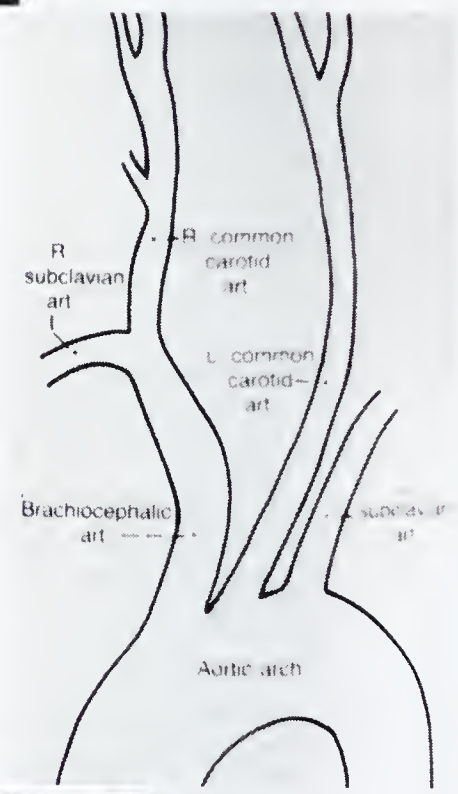


Fig. 2 An diagrammatic sketch of the arteriogram with all major vessels labelled.

Fig. 3 Diagram showing the spatial relationship of the major head and neck arteries.

Consideration Of The Natural Progression From Life To Death

Blake Croll Papsin, B. Sc., M. Sc., 8T8

The trip to the wards is training, understanding of it, a life's work. You find an unflattering blue smock, with a wearer usually tired, equally beaten. I recently met a man near death, excused his family from the bedside and conducted the fourth interview, according to him, of the day. My examination of his chest required that he breathe deeply, which he did until this manoeuver and morphine made him vomit. "It isn't your fault" and "I'm sorry" he said. I was uncomfortable with his apology because in a way it was my fault. I was sorry.

I have grown believing that sickness and death are naturally and simply related to life. That this relation is not clear in practice indicates a need for consideration. What forces distort the natural progression from life onward?

I believe my being there was right. This gentleman showed me great strength and dignity that afternoon, more impressive in the presence of suffering and the proximity to death. Since I left his beside I have wondered what right I had to benefit, as I surely did, from this moving moment.

In the sphere of my education thus far, the portion of life when mortality is waning, is not always welcome. I am, after all, taught preservation of life and function. I am upset initially because I am facing the experience of suffering and death for the first time but secondarily because I feel that problems associated with the smooth transition from life onward are somehow obscured by the intervention of medical science. An ethical rather than a microbacterial nosocomial infection.

This short essay is my attempt to explain how sickness and death have become so unnatural and to determine how much of the misunderstanding is the fault of Medicine at the bedside and in the classroom. This is not a discussion of when intervention is indicated or appropriate. That I trust, will come later in the course of my training. Nor will this paper shield my underclassmen's eyes from the first direct sun of a winter morning, so low in the sky. It is merely a shade for those who choose it, to allow emotional vision to remain acute amid the brightness. I hope this paper will provide a challenge to my peers, a plea to my teachers.

> To clean a trout. 1) Slit from the anal pore, up the belly to the cartilage near the gills. 2) With the tip of the blade scrape out the abdomen then slit the esophagus as close to the neck as you can. Alternatively, you can just cut along the backbone at the neck. As soon as you cut the head off the guts come out with it. 3) Slit off the fins then slit carefully down the back on either side of the backbone staying just lateral to the ribs all the way back to the tail. 4) Lay the fillet, skin down on a board (a paddle works just fine) and place the knife between the flesh and skin and cut towards the head in short cuts. 5) Don't forget the cheeks if the fish is bigger than 15 inches.

Here by the stream the cyclical, balanced view of life and its end prevails. The water thunders down the chute and each breeze full of August spray jolts you, makes you swear the sky just got bluer . . . again. Baudelaire in *Les Paradis Artificiels:* "La mort . . . nous affecte plus profondément sous le règne pompeux de l'été," (Death is more profound under the reign of summer). Today he is wrong.

The life that tugs my line from within that eddy is with me, on a single line of experience. The fish's passage to my dinner table, if I am in need of nutritive company doesn't enhance the profundity of the fish's death rather, as the end can be progressively traced, the transition is balanced. My conscience and full belly promote sleep. It would be improper to equate the fish's death with that of a patient but the clarity of the experience lends itself to study. The lesson learned by the stream is that a clear understanding of death is facilitated by experiencing the direct connection between life and death.

Philosophy and Western religion have considered life to have direction, a beginning and an end.

Birth is a beginning
And death a destination
And life is a journey:
From strength to weakness —
  And often back again;
From health to sickness
  And back, we pray, to health again
From pain to compassion
And grief to understanding —
  From fear to faith;
From defeat to defeat to defeat —
Until, looking backward or ahead,
We see that victory lies
Not at some high place along the way,
But in having made the journey, stage by stage,

A sacred pilgrimage
Birth is a beginning.
(Rabbi Alvin I. Fine 1916)

A physical model of this view could be a circle. Now, as a result of my limited medical experience I perceive it instead to be one complete turn of a coil with free ends disjointed. A break has occurred in the natural circumferential progression. Medicine contributes to the discontinuity first by breaking the linkage between life and death and second by interfering with the normal interpersonal relations necessary in concluding corporeal relationships.

The interruption of the linkage between life and death is easier to conceptualize and therefore will be considered first. To explain this discontinuity we must examine a tiny portion of the circle. When viewed miscroscopically like this, as is often done in Medicine, life's course is represented by a line. At this level Medicine clearly differentiates between life and death making continuity impossible. For example, the anaesthesiologist defines lines that leave and then rejoin the lifeline. Success as an anaesthesiologist is dependent on the ability to manipulate these travels in a predictable fashion. Levels of enzymes similarly may diverge from normality and return. Western Medicine is structured on the basis of health being the norm, sickness and death, deviations. The difficulty arises when we venture where these lines diverge permanently.

No longer is the life line connected with death as secular and philosophical literature has espoused. Medicine can interrupt the natural line connecting life, sickness and death for our benefit, for example, in the case where life is prolonged in a dying patient to allow the family to gather. However any interruption complicates the relation, structurally, as if replacing an arch with an arris.

Near death, when asked by a pious relative if he had made peace with God, Henry David Thoureau replied, "I am not aware we ever quarrelled." Last words today are often about how uncomfortable the treatment is. Don't misunderstand. It must be realized that had treatment for acute tuberculosis existed in 1860, Thoureau would have had twenty or thirty more years to say witty things. "No man had a better unfinished life" wrote his friend William Ellery Channing. The prolongation of life besides being of great value can interject an artificial pause thus contributing to the discontinuity which at present unnerves me. Medical technology can now describe definable space between two events once temporally connected.

It cannot be denied that this same technology contributes to improvements in the quantity and quality of life. Bruno Bettelheim, in *The Informed Heart*, suggests "that scientific and technological progress has relieved modern man of having to solve so many problems that he once had to solve by himself if he meant to survive, while the modern horizon presents so many more choices than it used to." Medicine through its technology, can offer improvements in life and function but can paradoxically strip the patient of his autonomy, by excluding him from decisions regarding the use of this technology.

Improvements in life and obscuration of the boundries of death are edges of the same blade, forged from the metal which knowledge fires. Medicine is required to shape the steel in order to meet the varied needs of family, conscience, definitely government and maybe even God. For this task we are not given introductory courses in blacksmithing. Our society meanwhile is flying to the moon.

The second way in which Medicine interrupts the linkage between life and death is by blurring the innate interpersonal relations between patient and family. Konrad Lorenz in his book *On Aggression* hypothesizes that the evolution of an inhibitory mechanism preventing sudden manslaughter of the members of one's own species was not necessary in humans because they had developed submissive gestures to elicit pity from potential aggressors instead. These gestures required contact between the parties involved in order to be effective. Lorenz suggests that the introduction of artificial long distance weapons made this innate protective mechanism obsolete. The introduction of technology into the innate behaviours associated with relationship ending may interfere with this interaction in a similarly destructive manner. I believe this occurs because the protective mechanism is similar to the process of ending a relationship in that they both require direct experience for success. Though machines may obscure interpersonal relations, judicious use of them must realistically continue. Great care in considering the interpersonal relation must be exercised.

In the realm of Medicine, the proud are those that fight. In the fight, the grieving process is put on hold by a continuous procession of medical staff and trainees flowing into the room signalling to the family that hope still exists. This delays the beginning to the process of concluding a relationship.

C.S. Lewis, describes the ending of a relationship with his wife in his book *A Grief Observed* as a process that needs maximal real information to be successful. This, he says, is critical because mourners are limited in their ability to process information and for this reason more than usual must be supplied. He describes his mourning psyche as consisting of,

> Five senses; an incurably abstract intellect; a haphazardly selective memory; a set of preconceptions and assumptions so numerous that I can never examine more than a minority of them, never becoming even conscious of them all. How much of

total reality can such an apparatus let through?

Questioning and subjective organization of sensory data allow the mourners to rejoin reality. Is a lounge on a ward or a hallway, while students conduct their interviews, a proper place for organization of thoughts? Are we supplying all the information we can? At the very least we should not cover up what little is available by our valiant defiance of disease.

Much of the important information can be transferred by the patient to his loved ones when he is fully aware of his situation. The problems with our medical system are not as severe as those described in Solzhenitsyn's novel *Cancer Ward* where patients are deliberately kept in ignorance of their status. The head Oncologist, Ludmila Afanasyevna Donstova, when asked by a patient why she had the right to assume what treatment each patient would want responded, "Doctors are entitled to that right — doctors above all. Without that right there would be no such thing as Medicine."

Giving patients back their autonomy would require more time spent with each patient explaining options, not less, as the government suggests. The patient's autonomy must be fiercely protected especially at the time when he or she is near death and trying to end mortal relationships. It is a dilemma that this is the time when modern Medicine is most involved and most potentially disruptive.

It is Christmas morning and I am in the palliative care unit of St. Michael's Hospital. By sheer luck or engineering genius the sun fills the rooms. Horticulturists would sell their souls for this southern exposure. The victrola is playing Christmas songs and several women are having their hair done and dressing up for the visitors that will be by later in the day.

On the first Wednesday after entering this unit the family and the patient meet with the medical and nursing staff in addition to a social worker. The patient's imminent death is discussed. The continuity between life and death is restored. The patients spend their last days comfortably and valuably with their family members.

I returned to the unit in the new year to see my friends and found six of ten had passed away, some within hours of sharing their lives with me. Here in this unit, death is accepted as an integral portion of life. More than steel fire doors separate this unit from the rest of the institution and the prevailing attitudes of modern medicine.

Acknowledgements

I would like to thank my Family, Dr. M. Greenberg and Dr. P. Kopplin for their analyses of the paper and Sandy for her thematic and grammatical contributions.P. Kopplin for their analyses of the paper and Sandy for her thematic and grammatical contributions.

Bibliography

The Informed Heart, Bruno Bettelheim (1960).
A Grief Observed, C.S. Lewis (1961)
On Aggression, Konrad Lorenz (1963).
Cancer Ward, Alexander Solzhenitsyn (1969).
Walden, Henry David Thoreau (1854).

For All Medical Students
Address UofT
Date October 84

℞ The finest in diagnostic and medical products, all on display in our showroom. — Just waiting for you.

Some Of Our Quality Brands:
Welch Allyn
Taylor (Tycos)
3M (Littmann)
Baum
Ritter
Miltex Instruments
Burdick

Take the subway — Osgoode Stop
10% discount with student card

Hours: 9:00 — 5:00
WHITE CROSS SURGICAL INSTRUMENTS LTD.
241 Richmond St. W., Toronto. M5V 2W3 (Tel. 598-4571)
5155 Timberlea Blvd., Mississauga (Tel. 625-2112)

FOR BETTER NUTRITION, PLEASE GIVE TO CARE CANADA

CARE®

CARE Canada
1312 Bank, Ottawa K1S 5H7

The Psychological Effect Of Mastectomy On Women

Pamela Stewart, 8T7

The Psychological Effect of Mastectomy on Women
Every year breast cancer strikes about eighty-five out of every one-hundred thousand white women in United States. Reported incidence of breast cancer appears on the rise. Indeed, it has been estimated that breast cancer will develop in approximately one of every fourteen women sometime during her life-span. With the etiology of cancer still uncertain, and the treatments still controversial both in their efficacy and their long-term psychosocial effects, it becomes important to evaluate the risks and benefits of each approach to breast cancer. This paper will examine the literature on the psychosocial effects of one form of treatment, mastectomy, on the women involved. The population of women examined will be largely caucasian (protestant or Jewish) reflecting the population at risk. Socio-economic status and its effects will not be studied, as most literature published up to date has examined a middle-class population. There will be little attempt to study the added repercussions of radiation or chemotherapy or even the different forms of mastectomy on the women's adjustment. Alternative treatments such as lumpectomies and breast reconstruction will only be considered to highlight the problems specific to women with mastectomies versus other forms of treatment. This paper will also briefly examine the implications of mastectomy as metaphor has for women in this society. The psychosocial effects of mastectomies on women could be categorized under two major headings: 1) a sense of mutilation, linked with a fear of death 2) a loss of feelings of femininity and hence concern over sexual desirability, interpersonal and sexual relationships and its relation to and impact on marriage. According to Maguire, these two principle effects of mastectomies create two major hurdles for women: one: to cope with the fact that every time they wash, bathe, undress, or look in a mirror, they may be reminded that they have had and may still have a potentially fatal disease and two: to adjust to being deprived of a part of their body that may have been of critical importance to their self-image, self-esteem and attractiveness to other people, especially their husband, friends and close family (1). Not only do these two factors and the hurdles they impose interlink, but they can also cause further conflict. For instance, mastectomy can be viewed as a temporary, at the very least, triumph over death. Consequently, feelings of sexual deprivation can create guilt in a woman who feels she ought to be grateful for the salvaging of her life. One post-mastectomy patient was quoted as saying: I wish all I had to worry about was whether my scar shows in a bathing suit, or if I can pick up a ten bag of sugar. Who in her right mind would be worried about being appealing when she finds out she's got cancer (2). Conspicuous in her comment is the dismissal, even, denial, of the right to feel grief over a loss of sexual identity. But as Asken points out in his discussion of the literature on the psychoemotional aspects of mastectomy: While mastectomy performs a gratifying service by saving a woman's life, her appreciation is muted by the price she must pay for that service - the loss of a breast and the permanent disfigurement. Within the value system of American society the price is an enormous one (3). Indeed, many women react to the amputation of a breast as a mutilating assault on femininity (4). And another post-mastectomy patient admitted: It (the mastectomy) made me heavily middle-aged; it forced me to throw away that part of my life in which I enjoyed my body with all its connotations of sexual freedom. I couldn't feel grateful for life. I realized I had been snatched from death, but I still didn't feel grateful (5).

The Psychological Effect of Mastectomy on Women
Every year breast cancer strikes about eighty-five out of every one-hundred thousand white women in United States. Reported incidence of breast cancer appears on the rise. Indeed, it has been estimated that breast cancer will develop in approximately one of every fourteen women sometime during her life-span. With the etiology of cancer still uncertain, and the treatments still controversial both in their efficacy and their long-term psychosocial effects, it becomes important to evaluate the risks and benefits of each approach to breast cancer. This paper will examine the literature on the psychosocial effects of one form of treatment, mastectomy, on the women involved. The population of women examined will be largely caucasian (protestant or Jewish) reflecting the population at risk. Socio-economic status and its effects will not be studied, as most literature published up to date has examined a middle-class population. There will be little attempt to study the added repercussions of radiation or chemotherapy or even the different forms of mastectomy on the women's adjustment. Alternative treatments such as lumpectomies and

breast reconstruction will only be considered to highlight the problems specific to women with mastectomies versus other forms of treatment. This paper will also briefly examine the implications of mastectomy as "metaphor" has for women in this society.

The psychosocial effects of mastectomies on women could be categorized under two major headings:

1) a sense of mutilation, linked with a fear of death 2) a loss of feelings of femininity and hence concern over sexual desirability, interpersonal and sexual relationships and its relation to and impact on marriage.

According to Maguire, these two principle effects of mastectomies create two major hurdles for women: one: to cope with the fact that every time they wash, bathe, undress, or look in a mirror, they may be reminded that they have had and may still have a potentially fatal disease and two: "to adjust to being deprived of a part of their body that may have been of critical importance to their self-image, self-esteem and attractiveness to other people, especially their husband, friends and close family" (1).

Not only do these two factors and the hurdles they impose interlink, but they can also cause further conflict. For instance, mastectomy can be viewed as a temporary, at the very least, triumph over death. Consequently, feelings of sexual deprivation can create guilt in a woman who feels she ought to be grateful for the salvaging of her life. One post-mastectomy patient was quoted as saying:

> "I wish all I had to worry about was whether my scar shows in a bathing suit, or if I can pick up a ten pound bag of sugar. Who in her right mind would be worried about being appealing when she finds out she's got cancer" (2).

Conspicuous in her comment is the dismissal, even, denial, of the right to feel grief over a loss of sexual identity. But as Asken points out in his discussion of the literature on the psychoemotional aspects of mastectomy:

> While mastectomy performs a gratifying service by saving a woman's life, her appreciation is muted by the price she must pay for that service — the loss of a breast and the permanent disfigurement. Within the value system of American society the price is an enormous one (3).

Indeed, many women react to the amputation of a breast as a "mutilating assault on femininity" (4). And another post-mastectomy patient admitted:

> "It (the mastectomy) made me heavily middle-aged; it forced me to throw away that part of my life in which I enjoyed my body with all its connotations of sexual freedom. I couldn't feel grateful for life. I realized I had been snatched from death, but I still didn't feel grateful"(5).

Indeed, a pervading feeling of mutilation, of invasion, of a presaging feeling of death still comes under major consideration. One woman comments:

> "The only data my brain registered were that breast cancer with metastases has only a short-term survival rate and I was mutilated. From the moment my physician said that I had metastatic breast cancer until two years after my surgery, I was frozen with fear. The people who are supportive were so shaken by my unexpected reaction that they ceased to function for me. The threat of death hung over me day by day, but I believe that mutilation was more traumatic. Living became so arduous. I found myself preparing to die on all levels — I stopped buying clothes or refurnishing my home as needed. Finally, I developed a speech pattern which became death-oriented" (6)."

What this patient describes is very similar, one imagines, to the feelings a person might experience in a war-time state of seige, where mutilation and death are daily realities. The difference lies in, where there is a war, in the traditional sense, there is usually an armistice day, the ready flying of the white flag of capitulation, of peace. In the fight with breast cancer, of which mastectomies become a visible reminder, there is no armistice, only temporary capitulation. And total capitulation, as this patient clearly indicates, can mean death.

Indeed, Susan Sontag, in her work, *Illness As Metaphor*, describes cancer as a metaphor in our society of hidden, military invasion, where the patient is both the territory invaded, and the prisoner of war. She says:

> The controlling metaphors in description of cancer are, in fact, drawn from the language of warfare: every physician and every attentive patient is familiar with, if inured to, this military terminology. Thus, cancer cells do not simply multiply; they are "invasive" ("Malignant tumours invade even when they grow very slowly" as one textbook puts it). Cancer cells "colonize" from the original tumour to far sites in the body, first setting up tiny outposts ("micrometastases") whose presence is assumed, though they cannot be detected. However "radical" the surgical intervention, how many scans are taken of the body landscape, most remissions are temporary; the prospects are that "tumour invasion" sill continue or that rogue cells will eventually regroup and mount a new assault on the organism (7).

Taking Sontag's discussion of cancer as military metaphor, then, mastectomy, as a treatment against the invasion of cancer explicitly represents both an abdication of territory (the "lost" breast) and a military battle for the control of a life-threatening disease. Thus, battle and disease become symbolic correlates. What is initially asked, in psychological terms, of all women who suffer from breast cancer, then, is an adjustment to the continuous state of war. If one peruses military literature, one

is struck by the description of prisoners who face surrender of themselves in the war. David Kentsmith in Military Medicine describes four stages of prisoner's of war's adjustment to his/her new status.

First, in the first stages of captivity, there is the question of "why me" or "how did this happen" or "what went wrong". These queries are interspersed with thought about "why me" are of guilt or remorse that life was not lived more fully or better when the person was free. "Some captives", Kentsmith continues, "even toy with the ideas that what has happened is "punishment" for their own thought. In the second stage of captivity the prisoner of war spends hours even days over the loss of personal freedom and the new physical restraint he feels. As the captivity continues, the prisoner typically develops anxiety about further injury or death. Finally, Kentsmith concludes, the point finally arrives, however, when the captive is able to answer the question "why me", is about to resolve the guilt and remorse over things lost, and to accept his mortality and the fact he might die. More specifically, however, eventhough "there is a philosophical acceptance of his dilemma, he continues to struggle with inability to control his own destiny" (8).

Literature on Post-mastectomy adjustment reflects, in various degrees, these four stages of adjustment. Morris et al describe the responses to mastectomy by women as anxiety ("why me"?), depression, anger, guilt, fear of death, regression and denial (9). Similarily, Renneker and Culture, who studied post-mastectomy responses in 50 women, found post-mastectomy depression marked by anxiety, insomnia, depressive attitudes, occasional suicidal ideas, and feelings of worthlessness and shame (10). In most studies, there is a sense of abdicated power, of freedom lost, and the fight for survival, true of any state of war. Indeed, military idiom creeps into the language post-mastectomy patients use to describe their emotional state. Sheila Kitzinger quotes Audre Lorde as saying:

> "For me, my scars of mastectomy, are an honourable reminder that I may be a casualty in the cosmic war against radiation, animal fat, air pollution, Macdonald's Hamburger and Red Dye Number 2; but the fight is still going on and I'm part of it. I refuse to have my scars hidden or trivialized behind lamb's wool or silicone gel. I refuse to be reduced in my own eyes or in the eyes of others from warrior to mere victim" (11).

In literature, where the basic underlying realities of society's views are twisted open to reveal their inner metaphors, Margaret Atwood in her novel, *Bodily Harm*, equates the state of mastectomy to a country under the state of seige, where everyone involved faces the implications of danger, death, guilt and shame. Cancer, like political coups, was a "front-parlour subject, but it wasn't in the same class as a broken leg or a heart attack or even a death. It was apart, obscene, almost, like a scandal; it was something you brought upon yourself" (12). Finally, implicit to the meaning of war, is life atrophied, circumvented, mutilated. And it is the feeling of mutilation, as much as, or even more than the threat of death that affects the post-mastectomy patient. Indeed, Maguire reports that women commonly used phrases and words such as "second class", "below standard", "mutilated", "peculiar", "lopsided", "abnormal", "so inadequate" to describe how they felt after surgery.

But whereas, possibly, all cancers, regardless of their location, may create that state of war, the feeling of a slowly eroding mutilation, when one studies the psychosocial effects of breast cancer, the sexual implications for women are far greater, perhaps, than any other cancer, more so, some feel, than cancer of the ovaries, vagina, cervix, or uterus, since breasts are a more visible symbol of women's femininity. For the breast, in our society, is viewed as a symbol of sexuality and fertility. Mastectomy, then, is viewed, at least subconsciously, as a loss of sexual identity, a diminishing of sexual worth and marketability. As Janet Polivy points out:

> The effects of mastectomy would be expected to differ from other surgery because of the sexual implications of the loss of a breast and its potentially devastating effect on a woman's self-image and physical attractiveness, especially in our breast-conscious society (14).

There are numerous studies on the effect of this loss of feminine identity on feelings of self-esteem, self-worth, and consequent psychiatric morbidity, which includes depression lasting weeks even years and thoughts of suicide. The extent of the reaction of post-mastectomy patients, seems, to be, partially, if not strongly predicated upon 1) their age at the time of mastectomy; 2) the amount of support offered them by family, friends, physicians and husbands and 3) their marital status and stability, if married, of their marriage before the event of the mastectomy.

Though there are some differences in opinion, most studies concluded that the women most affected, in terms of psychiatric morbidity and consequent decline in self-esteem, were those in the pre-childbearing state and those in their middle years or climacteric women. These stages coincide with Gail Sheehy's two crucial passages in the life of a woman. Gail Sheehy writes:

> During each of these passages, how we feel about our way of living will undergo subtle changes in four areas of perception. One is the interior of self in relation to others. A second is the proportion of safeness to danger we feel in our lives. A third is our perception of time — do we have plenty of it or are we beginning to feel that time is running out? Last,

there will be some shift at the gut level in our sense of aliveness or stagnation. Theses are the hazy sensations that compose the background tone of living and shape the decisions on which we take action (15).

Naturally, an additional outer stress, such as both breast cancer, and mastectomy, throws all these "sensations" into sharp focus. Sheehydescribes the initial child-bearing, or premarital stages as the "Trying Twenties" where our focus shifts from "the inner turmoils of late adolescence, "Who am I", "What is truth" — to "a preoccupation with working out the externals i.e. How do I put my aspirations into effect" (16). Aspirations, of course, include marriage, career, and self-actualization, all of which could be seen to be considerably curtailed by the reality of not only breast-cancer, but of a semi-mutilated already scarred self. Indeed, Lavis et al postulated that younger women react more to the loss of the breast itself, whereas older women find the adjustment to cancer harder (17). Maguire also makes the distinction that most older women were predominantly concerned with survival and the possible suffering involved rather than actual breast loss (18). Maguire also comments:

Older women, particularly those aged 60 or over whose interest in sex had already declined naturally, who had understanding husbands, or close friends they could confide in, and who did not place great value on their busts adapted fairly readily. In contrast, young women for whom an active sexual relationship was still important, who considered their busts essential to their attractiveness . . . found it hard to adjust (19).

However, the Goins in their study of mid-life reactions to mastectomy cautioned against the assumption that older women had declined in sexual interest. Indeed, they urge that women in that age-group would be more hesitant to admit decreased sense of sexuality since it might be seen as socially inappropriate to their age-group, and hence not recognized by either interviewer or various support-systems (20). Paula Weidegner in *Female Cycles*, describes the dilemma of the post-climacteric woman:

Theoretically, at least, women are able to have a more rewarding sex life after menopause. No doubt many women are enjoying the fruits of their age even while acting if sex were the last thing that interests them. Many other women may indeed lose interest in sex simply because they believe that it is what ought to be happening to them at "that time of life" (21).

Obviously given the cultural confusion over what is sexually expected of post-climacteric women, a more in-depth, discerning study of post-climacteric women might still be needed.

The second age-group most affected psychosocially by mastectomies is the age-group 45-65 years of age. Again, this is a period of transition or passage. Marcia Goin et al did an interesting study of this age-group. They studied the reactions to mastectomies of a group of middle-aged women who were aware of the possibility of surgical reconstruction of the breast and were considering that an option for themselves. The authors admitted a selection-bias in that they only interviewed patients who wanted a surgical reconstruction and, therefore, perhaps skewed the studies in terms of their own "possible" maladjustment to mastectomy. Nevertheless, faced with the possibility of an alternative, these women would also be possibly more willing to share their emotions. Goin et al interviewed 17 women in all, the majority of whose ages lay between 45-65. None of the women were single; one was separated, one divorced, and eight were married. Goin et al found the reactions of these women to progress through anger, denial, despair and acceptance. However, they found the majority of the 45-54 age-group by-pass denial, anger and despair, to a feeling of pseudo-acceptance. Most women had feelings of depression, but hid them well, feeling them to be, as one patient termed it "disgusting feelings of self-pity". They experienced feelings of sadness and crying spells, as well as a decrease in sexual desire. Indeed, they felt it "ludicrous" to think of themselves as sexually desirable. Outwardly, the women were seen to cope well, back at work or volunteer activities within weeks of their mastectomies. Families and friends were consequently astonished by the women's desire for breast-reconstruction. Fears of and a fight against dependency were themes that cropped up continuously in interviews. Goin et al quoted on patient as saying:

"Now I don't have to fear that my husband is staying with me out of pity. He could leave me if he wanted to , knowing I could take care of myself" (21).

Two of the women interviewed denied any feeling of loss until they were confronted with some life-changes. Clearly, these were issues that could have been missed if breast-reconstruction did not offer the possibility of an alternative to their present choices.

Goin et al saw the middle years as a crossroads at which both men and women confront their fear of dependence, concerns of loss of income, and deteriorating health. It is consequently a period where they take a strong investment in physical appearance and functioning. It is a time of social and psychological assessment and reorganization and possibly for women particularily a time of new careers. Therefore, Goin et al state that the "middle-aged woman with breast cancer faces a major body mutilation just at the time when she is experiencing heightened anxiety about physical attractiveness, declining health and fears of dependence"

(22). These senses of mutilation, loss and fear of dependence are superimposed on the mid-life anxiety. Goin et al stressed how important it is to appreciate the older woman's shame about her feelings of loss following mastectomy; how she might deem it inappropriate to express her sense of sexual loss, and assumptions by well-meaning physicians could lead to a misunderstanding of her needs.

The other major influence on the psychiatric morbidity of post-mastectomy patients was, as mentioned, the stability of their marriages. C. Dean et al did a study on 64 women to assess psychiatric, sexual, social, marital and work morbidity. 31 women were allocated to no implant after mastectomy; 33 women were given immediate implantation. What they discovered was that psychiatric morbidity was significantly decreased in women with implants after three-months, only if they faced unhappy marriages. Similarily, a study in *JAMA* comparing the psychological impact of lumpectomies to mastectomies found sexual dysfunction only in those who had marital problems before surgery (24). However, regardless of age or marital status, most studies report some social and sexual decline of activity of women with mastectomies. Jamieson et al did a study on the psychological effects of mastectomy on 41 women. 16 of the women were under 45 years old and 25 were over 45 years old. 80% of the women were married. ¼ of the women experienced suicidal ideation; 1/3 of them took increased doses of tranquilizers and 15.4% significantly increased their alcohol intake. Eighty-nine per cent of them spent little time talking about the emotional aspects of mastectomy with either the spouse or significant other. 50% of the women still did not discuss their feelings after going home. Sexual relationships varied, but on the whole decreased. Younger women rated their post-mastectomy adjustment as significantly poorer. A higher number of the less than 45-age group also sought psychiatric help. The factors at play seemed to be age, presence of support systems and level of premastectomy functioning. Jamieson et al stressed the need for counselling of both partners prior to and after mastectomies (25).

Finally, as an ambivalent impact on a post-mastectomy patient's self-image is, perhaps, surprisingly the presence of the other breast, in the case of unilateral mastectomies. Leis points out that much is "made of the psychological importance of the remaining breast, which may be cherished as a badge of motherhood, a sign of femininity and an important psychosexual symbol". Yet, he continues:

> . . . the second breast remains a non-functioning organ; few women display it as a "questionable" sexual stimulus next to a mastectomy scar, and few allow it to be used during the sexual act. Some doctors will not permit the remaining breast to be used in breast-feeding, there is also the problem of disrupted body symmetry. Finally, patients may live with the fear of recurrent cancer in the remaining breast. Thus, the breast has both a positive and negative value to the patient resulting in vacillating ambivalence (25).

In conclusion, the effects on a woman post-mastectomy appear to be two-fold: one: a sense of mutilation and two: a loss of femininity. These effects could be best ameliorated by adequate counselling of patient and family, a clear and trusting liaison with the phsician, a clear idea of options of treatment (especially as lumpectomies are now emerging as the treatment of choice in many cases with lower associated psychiatric morbidity) and a defined support system. As one patient so eloquently put it — all a post-mastectomy patient needs is the four "F's": "faith, family, friends and ph(f)ysician".

END-NOTES

1. **Peter Maguire, The Psychological and Social Consequences of Breast Cancer;** *Nurs. Mirror.* 140:55, 1975.
2. Rose Kushner, *Alternatives.* Kensington Press. Mass. 1982. p.333
3. Michael Asken, Psychoemotional Aspects of Mastectomy: A Review of Recent Literature; American Journal of Psychiatry. 132:1, January 1975:56.
4. Fitzpatrick, Renneker, Cutter quoted in Janet Polivy: Psychological Effects of Mastectomy on A Woman's Self-Concept, *The Journal of Nervous and Mental Disease.* 164:78, 1977.
5. Sheila Kitzinger, *A Woman's Experience of Sex.* Penguin Books; London, England. 1983. p.308
6. Michael J. Asken. p.56
7. Susan Sontag, *Illness as Metaphor.* Farrar, Straus and Giroux. New York. 1978. p.648.
8. David K. Kentsmith; Hostages and Other Prisoners of War. *Military Medicine.* Vol. 147:969-970. Nov. 1982.
9. quoted in Janet Polivy: p.79
10. *IBID.*
11. Sheila Kitsinger: p.308
12. Margaret Atwood; *Bodily Harm.* McClelland and Stewart-Bantom Ltd., Toronto. 1981: p.82
13. Peter Maguire; p.55
14. Janet Polivy: p.78
15. Gail Sheehy; *Passages*: Predictable Crises of Adult Life. Banton Ltd., New York. 1976: p.30
16. *IBID*
17. Frances Lewis et al; Psychosocial Adjustment to Breast Cancer: A review of Selected Literature. *International Journal of Psychiatry in Medicine.* 9:15. 1975.
18. *Ibid*
19. Peter Maguire: p.56

20. Marcia K. Goin; Midlife Reactions to Mastectomy and Subsequent Breast Reconstruction. *Archives of General Psychiatry*. 38:227. 1983.
21. *IBID*
22. *IBID*
23. C. Dean et al: Effects of Immediate Breast Reconstruction on Psychosicial Morbidity After Mastectomy. *Lancet:* Geb..26(8322); 459, 1983.
24. J. Konn; Psychological Impact of Two Types of Breast Cancer Surgery. *JAMA*. 248(15)459: 1982.
25. Kay R. Jamieson et al; Psychosocial Aspects of Mastectomy I: The Women's Perspective. *American Journal of Psychiatry*. 135:432-436: 1978. 26. Quoted in Asken: 1.

BIBLIOGRAPHY

A spen, Michael J.; Psychoemotional Aspects of mastectomy: A Review of Recent Literature. *American Journal of Psychiatry*. 132:1; January 1975.

Atwood, Margaret; *Bodily Harm*. McClelland and Stewart-Bantom Ltd., Toronto 1981.

Boyd, Peggy Phd.; *The Silent Wound: A startling Report on Breast Cancer and Sexuality*. Addison-Wesley Publishing Co., Mass., 1984.

Christensen, K. et al; Phantom Breast Syndrome in Young Women After Mastectomy for Breast Cancer. *Acta Chir. Scand.* 148(4):351-4, 1982.

Dean, C. et al; Effects of Immediate Breast Reconstruction on Psychosocial Morbidity After Mastectomy. *Lancet*. Feb.26 (8322): 459-62; 1983.

Goin, Marcia and Goin, John M.; Midlife Reactions to Mastectomy and Subsequent Breast Reconstruction. *Archives of General Psychiatry*; 38:25-227, 1981.

Jamieson, Kay R. et al; Psychosocial Aspects of Mastectomy I: The Woman's Perspective. *American Journal of Psychiatry*. 135:433-436. 1978.

Kentsmith, David K.; Hostages and other Prisoners of War. *Military Medicine*. Vol. 147:969-972; Nov. 1982.

Kitsinger, Sheila; *A Woman's Experience of Sex*. Penguin Books, London, England. 1983.

Kushner, Rose; *Alternatives*, Kensington press. Mass., 1982.

Konn, J.; Psychological Impact of Two Types of Breast Cancer Surgery. *JAMA*. 248(15):559-61, 1982.

Lewis, Frances et al; Psychosocial Adjustment of Breast Cancer: A Review of Selected Literature. *International Journal of Psychiatry in Medicine*. 9:1-17, 1978-79.

Maguire, Peter; The Psychological and Social Consequences of Breast Cancer. *Nurs. Mirror*. 140:54-58, 1975.

Polivy, Janet; Psychological Effects of Mastectomy on A Woman's Self-Concept. *The Journal of Nervous and Mental Disease*. 164:177-187, 1977

Schoffenfeld, David; Quality of Survival Among Patients Who Have Had Radical Mastectomy. *Cancer*. 26:650-655, 1970.

Sheehy, Gail; *Passages: Predictable Crises of Adult Life*. Bantom Ltd., New York. 1976.

Sontag, Susan; *Illness as Metaphor*. Farrar, Straus and Giroux, New York, 1978

Tarrier, N. et al; Treatment of Psychological Distress Following Mastectomy: An Initial Report. *Behav. Res. Ther.*; 22(1):81-4, 1984.

Weideger, Paula; *Female Cycles*. The Women's press, London, England, 1977.

Wellishch, David R. et al; Psychosocial Aspects of Mastectomy:II: The

Man's Perspective. *American Journal of Psychiatry*. 135:543-546, 1978.35:543-546, 1978.

MEDICAL MART
SUPPLIES LIMITED

1224 DUNDAS STREET E., UNIT 28
MISSISSAUGA, ONTARIO, CANADA
L4Y 4A2 PH. (416) 276-4800
MEDIWATTS 1-800-268-2848 (ONT. ONLY),
TELEX 06-960218

PHYSICIAN STUDENTS SUPPLIES
A ONE STOP SUPERMARKET
FOR ALL YOUR OFFICE NEEDS

- Welch Allyn Diagnostic
- Treatment Cabinets
- Taylor & Brum B P Units
- Littmann Stethoscope
- B-D Syringes & Needles
- Step Stools
- Surgeon's Stools
- Exam Tables
- Scales
- Dressings

Let our experienced trade professional assist in your requirements

VISIT OUR LARGE MODERN SHOWROOM

HOURS: 9:00 - 5:00 Mon., Tues., Wed.
9:00 - 7:00 Thurs. 9:00 - 6:00 Fri.

Respirology Rounds — Answers

Diagnosis: Oat Cell Carcinoma of the Lung with the Syndrome of Inappropriate ADH

The chest radiographg (Fig. 1A, B) demonstrates atelectasis of the right upper lobe, however, in addition there is loss of the upward convexity of the medial aspect of the minor fissure suggestive of a mass in this area. Flexible fiberoptic bronchoscopy revealed a mas obstructing the right upper lobe bronchus. Histology of a specimen obtained by biopsy of this mass was compatible with small cell carcinoma of the lung. Urine osmolarity was 481 mosm/l, with a urine sodium of 31 mmol/l coincident with a serum sodium of 129 mmol/l and serum osmolarity of 257 mosm/l. Creatinine clearance was 1.2 ml/sec. Serum cortisol and thyroid function tests were normal.

This woman has the syndrome of inappropriate antidiuretic hormone (SIADH) in the presence of oat cell carcinoma of the lung. SIADH may be diagnosed in a patient who has serum hyposmolarity and hyponatermia and urine that is less that maximally dilute. Since these patients are either euvolemic or hypervolemic the urine sodium will match the sodium intake despite hyponatremia. This will happen because there is a excess of total body water in the presence of a normal total bady sodium. The body perceives the presence of extracelluar volume expansion which initiates natriuresis (via the usual hormonal and physical mechanisms. eg. suppression of aldosterone secretion and augmentation of physical factors permitting sodium excretion.

A diagnosis of SIADH can only be made in a patient who is clinically normovolmic. In addition the patient must not have any conditions which would result in an inability to dilute the urine normally. Consequently, there must not be a state where the body perceives intravascular volume depletion such as the edema forming states of heart failure, cirrhosis, hypoproteinemia or nephrotic syndrome. Causes of decreased diluting capacity of the kidney such as acute or chronic renal failure, hypothroidism or hypoadrenalism must be excluded.

Diseases associated with SIADH include malignancies, chronic pulmonary infections, central nervous system disorder such as trauma and infrecton and certain drugs. Stress itself can produce this syndrome. In rare cases no underlying cause can be determined. Fifty percent of the reported cases of SIADH have been associated with tumours. Oat cell carcinoma is almost always the cell type in lung tumour patients.

Antidiuretic hormone (ADH) is an octapeptide secreted from the posterior pituitary in response to changes in plasma osmolarity. This hormone is normally released in increasing amounts in response to increasing plasma osmolarity, and acts on the distal tubule and collecting duct portion of the nephron to

Fig. 1A

Fig. 1B

allow water reabsorption. In SIADH th normal control is deranged.

There are four patterns of ADH response in relation to plasma osmolarity in SIADH. In type A there are erratic changes in plasma ADH that bear no relationship to serum osmolarity. This pattern is seen with some tumours. In type B the threshold for ADH secretion is decreased but the normal relationship of increasing ADH release in response to increasing osmolarity is preserved. Thus there is an inappropriately high value of ADH present for any level of plasma osmolarity above the new threshold for secretion. In type C there appears to be a constant leak of ADH on top of an otherwise normal response. In type D the measured ADH is appropriate to the plasma osmolarity however the kidney response to the ADH is accentuated and kidney concentrates the urine to an inappropriate degree. This type has been described in the presence of oat cell carcinoma of the lung.

In this case the hyponatremia manifested itself five months prior to the diagnosis of oat cell carcinoma. This is uncommon, but does illustrate that a paraneoplastic syndrome may present itself well in advance of clinical detection of the underlying malignancy.

Our patient responded well to treatment with simple fluid restriction to 800cc per day and her serum sodium rose to normal within a week. In instances where hyponatremia is more profound, of more rapid onset or associated with neurological symptoms such as stupor or seizures, treatment should be undertaken with the administration of hypertonic (3%) saline. In addition cautions furosemide induced diuresis along with hypertonic of isotonic saline replacement may be required to more rapidly correct the serum sodium. Persistent hyponatremia unresponsive to more simple treatments can be managed with demeclocycline which results in resistance to the action of ADH at the level of the renal tubule.

Oat cell carcinoma of the lung is staged as being either limited disease when it is confined to one hemithorax including ipsilateral scalene nodes, or extensive disease which includes all the remaining cases. The tumour tends to metastasize to regional lymph nodes, elsewhere within the lungs, abdominal lymph nodes, liver, adrenal glands, bone, central nervous system and bone marrow.

The prognosis of small cell carcinoma is very poor as it is usually disseminated at the time of diagnosis. Untreated median survival is about two months. With treatment, this increases considerably depending on the extent of the disease at the time of diagnosis. Treatment usually involves chemotherapy often in conjunction with radiotherapy.

Radiotherapy would be directed at localized lesions. In rare cases surgery would be considered for this tumour if it was felt to be localized only to the lung.

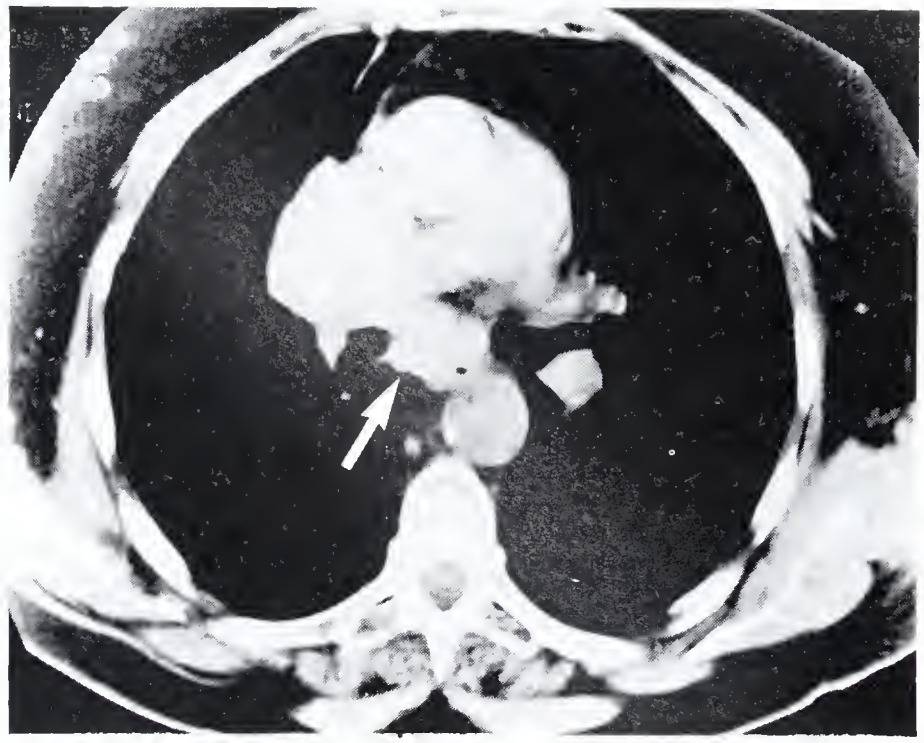


Fig.2

Staging investigations usually involve conventional chest x-rays and possibly tomograms or CT scan to define the extent of intrathoracic disease. Radioisotope bone, liver and brain scans define the presence of metastases of detectable size in these organs. Bone marrow aspiration and biopsy frequently shows metastatic small cell carcinoma. An alkaline phosphatase is helpful in identifying metastatic disease in liver or bone. CEA levels may be followed to monitor treatment. Mediastinoscopy would be used only in that rare case where surgery is considered.

In our patient a CT scan of the chest showed involvement of the subcarinal mediastinal nodes. (Fig. 2) A CT scan of the abdomen (not shown) suggested metastatic involvement of one adrenal gland as well. Bone marrow examination showed extensive tumour infiltration.

References

Martinez-Maldonado M. *Inappropriate Antidiuretic Hormone Secretion of Unknown Origin.* Kidney Int. 1980. 17: 554-567

Cohen IM, Warren SE, Skowsky WR. *Occult Pulmonary Malignancy In Syndrome of Inappropriate ADH Secretion with Normal ADH Levels.* Chest 1984; 86: 924-930

Rohwedder JJ. *Neoplastic Disease and Mediastinal Disorders.* In: Guenter CA, Welch MW. Pulmonary Medicine 2d edition. Philadelphia: J.B. Lippincott, 1982: pp 825-828

Van Houtte p, Salazar OM, Phillips CE, Asbury RF. *Lung Cancer.* In: Rubin P. Clinical Oncology 6th edition. American Cancer Society, 1983: pp 142-149.

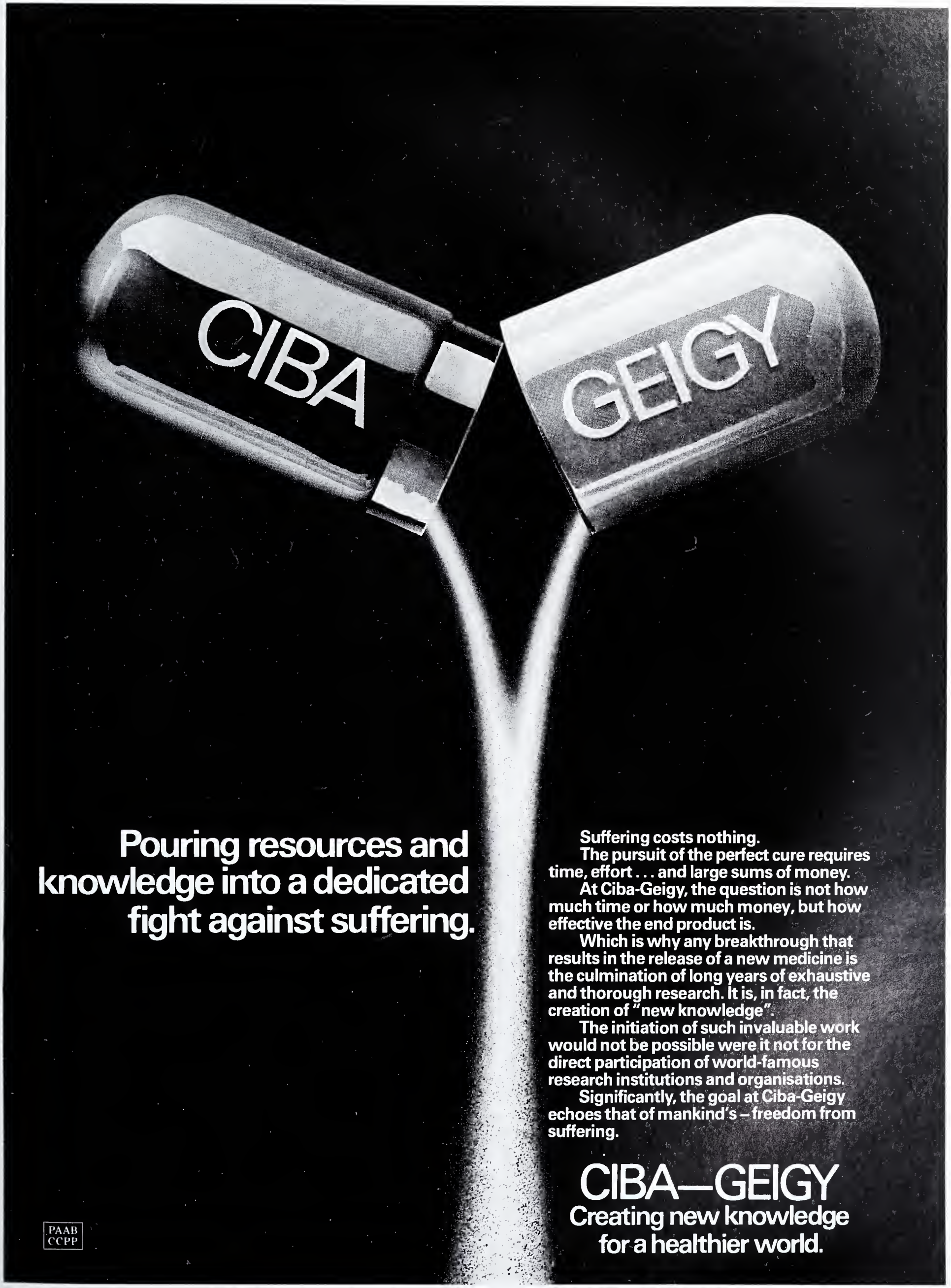
Patrons

The *Journal* staff and Medical Society wishes to thank the following patrons for their generous support.

Dr. Sharon M. Abel
Mrs. Elizabeth Akesson
Dr. Peter W. Alberti
Dr. E.C. Allen
Dr Dominick Amato
Dr. Ulo Ambus
Dr. William Anderson
Dr. Crawford S. Anglin
Dr. John Armstrong
Dr. Maria Arstikaitis
Dr. Sylvia Asa
Dr. Mary Jane Ashley
Dr. Ronald Baigrie
Dr. Michael A. Baker
Dr S Bandak
Dr Eric J. Barker
Dr Jack Barkin
Dr. S. Barker
Dr. Marshall Barkin
Dr. Martin Barkin
Dr. Peter Barreca
Dr. Alan A. Bassett
Dr. Colin Bayliss
Dr. R. J. Benzie
Dr. John A. Beswick
Dr. Barbara Blake
Dr. Charles Brown
Dr Peter Brueckner
Dr. Martin Buckspan
Dr. Gerald Burrow
Dr. David S. Byers
Dr. Paul Cameron
Dr. Lorie Cappe
Dr. John Cardarelli
Dr. D. C. Cattran
Dr. A. Cecutti
Dr. Abraham Chaiton
Dr. Catherine Chalin
Dr. Morris Charendoff
Dr. Albert T Cheskes
Dr. R. J. Chisholm
Dr. Bernhard Cinader
Dr. Robert Cleghorn
Dr. Max M. Cohen
Dr. Alan W. Conn
Dr. George Connell
Dr. John Connolly
Dr. Harvey Coopersmith
Dr. Robert Corringham
Dr. Donald Cowan
Dr. Carol Cowell
Mrs. Marie Crookston
Dr. Donald Currie
Dr Derek A. Davidson
Dr. John K. Davidson
Dr. Yvonne de Buda
Dr. Terence Doran
Dr Dale Dotten
Dr. James Dubbin
Dr. James Duffin
Dr Henry Durost
Dr Robert Ehrlich
Dr David Ellis
Dr Stanley Epstein
Dr Emmanuel Farber
Dr Shim Felsen
Dr Ronald Fenton
Dr Joseph Fisher
Dr K. Fleming
Dr. N. Forbath
Dr. Rodney Fowler
Dr. William Francombe
Dr Jeremy Freeman
Dr. Arnis Freiberg
Dr WW C. F. Forder
Dr. Gordon Froggatt
Dr. A. E. M. Geisler
Dr. Robert Ginsberg
Dr. Richard M. Gladstone
Dr. David M. Goldberg
Dr. Melvyn Goldberg
Dr. Michael R Goldberg
Dr. Barry Goldlist
Dr. Irvin Gollish
Dr. Maria Gospodarowicz
Dr. Avrum Gotlieb
Dr. Cameron C. Gray
Dr David Greyson
Dr. Allan Gross
Dr. Joseph Gruss
Dr Michael L. Guinness
Dr. Madhulika Gupta
Dr. Gordon Hardacre
Dr. Philip Halloran
Dr. Mitchell Halperin
Dr. & Mrs. Abraham L. Halpern
Dr. A W. Ham
The Hanna Institute
Dr. Walter Hannah
Dr. Ian Harrington
Dr. Robert V. Harrison
Dr. Gerald Heasman
Dr. E. B. Hendrick
Dr. F. M. Hill
Dr. Charles Hollenberg
Dr. Robert Howard
Dr. Michael Howcroft
Dr. Shao-Nan Huang
Dr. Paul Hwang
Dr. A. R. Hudson
Dr. Robin Humphreys
Dr. Gordon Hunter
Dr. M. Hutcheon
Dr. R. H. Hyland
Dr. Aden C. Irwin
Dr. Mary V. Jackson
Dr. Robert W. Jackson
Dr. Christopher Jamieson
Dr. Moray G. Jansen
Dr. Romana Januszewska
Dr. Michael Jewett
Dr. Donald P. Jones
Dr. Albin T. Jousse
Prof. Nancy Joy
Dr. Armand Keating
Dr. John Kempston
Dr. Margot Kempton
Dr. Thomas Keogh
Ms. M. Kemptone
Dr. James H. Kerr
Dr. Edward Keystone
Dr. Jay Keystone
Dr. Hollister King
Dr. Jurgen Kontor
Dr. John Kostuik
Dr. Bernard Langer
Dr. Wolf-Dietrich Leers
Dr. S. L. Librach
Mr. Sidney Liswood
Dr. Lynn Loach
Dr. Frederick Lowy
Dr. John Lundon
Dr. Elliot Lyons
Dr. Robert E. MacDonald
Dr. Ross C. MacKay
Dr. Robert Lee MacKenzie
Dr. Susan Mackinnon
Dr. Stuart MacLeod
Dr. Ian MacNab
Dr. Aaron Malkin
Dr. Dina Gordon Malkin
Dr. Constantine Mallin
Dr. Jaanus Marley
Dr. Joseph Marotta
Dr. A. Bruce Marshall
Dr. B. J. Massouda
Medical Emergency Services
Wellesley Hospital
Dr. Nancy McKee
Dr. Rosemary Meier
Dr. Kenneth R. Melvin
Dr. Peter Mingle
Dr. Charles A. F. Moes
Dr. Keith L. Moore
Dr. J. E. Morgan
Dr. Heather Morris
Dr. David Murray
Dr. James F. Murray
Dr. Neil McAlister
Dr. David McNeely
Dr. Salim Naqvi
Dr. Constant Nucci
Dr. Richard Oglivie
Dr. D. Oreopoulos
Library Ortho Pharmaceutical (Can.) Ltd.
Ortho Pharmaceutical (Canada) Ltd.
Dr. Howard Ovens
Dr. Frederick Papsin
Dr. Robert Patten
Dr. George Alexander Patterson
Dr. Thomas Patterson
Dr. F. R. Pember
Dr. Gordon A. Pengelly
Dr. Richard Perrin
Dr. W. J. Peters
Dr. Mel Petersiel
Dr. Annett Poon
Dr. Peter V. Poon
Dr. Kathleen Pritchard
Dr. John Provan
Dr. Vivian Rakoff
Dr. Anthony Rebuck
Dr. Robert N. Richards
Dr. Robin Richards
Dr. Kenneth Robb
Dr. Alexander Roberts
Dr. Robert Salter
Dr. Michael Schwartz
Dr. Arthur Scott
Dr. Edward e. Sellers
Prof. Patricia Seyfried
Dr. Shao-Nan Huang
Dr. Robert H. Sheppard
Dr. Jerry Shime
Dr. Jack Shuber
Dr. K. H. Shumak
Dr. Ruth Shykoff
Dr. Daniel Silver
Dr. Harley Smyth
Dr. G. E. D. Snell
Dr. Robert Snihura
Dr. Isaac Sokinofsky
Dr. Marja Soots
Dr. Donald A Stewart
Dr. Margaret Stoicheff
Dr. Robert Stone
Dr. Lorne Tarshis
Dr. Charles Tator
Dr. John Taylor
Dr. Ron Taylor
Dr. William Tucker
Dr. W. P. Unger
Dr. Joan Vale
Dr. Daniel G. Vaughan
Dr. Hillar Vellend
Dr. Malden Vranic
Dr. James P. Waddell
Dr. Paul Walfish
Dr. Gary D. Webb
Dr. R. K. Weber
Dr. Peter Webster
Dr. Richard Weisel
Dr. David Wesson
Dr. Catherine Whiteside
Dr. Robert H. Wilkinson
Dr. D. R. Wilson
Dr. Daniel Wise
Dr. & Mrs. Manley S. Wolochow
Dr. Colin Woolf
Dr. John Zeldin
Dr. Walter Zingg
Alpha Laboratory
Boots Drug Store
Burroughs Wellcome Inc.
Ciba-Geigy Pharmaceuticals
Hoffman La Roche
MDICL Inc.
Medical Alumni Association
Medical Bookstore
Medical Mart Supplies
Merck Frosst Canada Inc
Novopharm Ltd.
Searle Pharmaceuticals
Squibb Pharmaceuticals
W B Saunders
White Cross
Cytopathology Associates
Med-Chem Laboratory

(cont. from page 36)

12. Gotto A.M., et all 1977 atherosclerosis. Scope Publication. Kalamazoo Michigan
13. Thomson J.E, Talkengton GMM: Carotid Endarferectomy. Ann Surg 184:1-55, 1976.
14. Engel S; Ferraz H: Indicvation â Results of ECIC Arteral Bypasses. International Surgery
15. Chowdhavy WM: EC to IC Vascular Anastomosis For Ischaemic Cerebrovascular Disease. Irish Medical Journal 74 (10): 287-90, 1981.
16. Amaducci L, et al: The International EC/IC Bypass Study. Stroke 13 (2): 1982.
17. Chater, N, Results of Neurosurgical Microvascular Ec-Ic Bypass For Stroke. Western Journal of Medicine, 138(4): 531-3, 1983.
18. Gersten JW, Rehabilitation Potential. IN: Licht, S, ed; Stroke and its rehabilitation. Neew Haven: E Licht, 1975:425.
19. Lehamann JF et al, Stroke: does rehabilitation offset outcome? Arch. Phys. Med. Rehab., 56: 375, 1975.
20. Sacco RL, et al: Survival and Recurrence Following Stroke, The Framingham Study. Stroke 13: 290-295, 1982.
21. Hutchinson EC, Acheson EJ. Strokes Natural History, Pathology and Surgical Treatment. Philadephia; WB Saunders Co, 138-177. 1975.
22. Chater, N., Popp, J.: Microsurgical vascular bypass for oclusive cerebrovascular disease: Review of 100 cases. Surgical Neurology. 6:115-118 (1976).
23. Popp, A.J., Chater, N.: Extracranial to intracranial Vascular anastomasis for occlusive cerebrovascular disease: experience in 110 patients. Surgery. 82, No. 5: 648-654 (1977).



Pouring resources and knowledge into a dedicated fight against suffering.

Suffering costs nothing.

The pursuit of the perfect cure requires time, effort . . . and large sums of money.

At Ciba-Geigy, the question is not how much time or how much money, but how effective the end product is.

Which is why any breakthrough that results in the release of a new medicine is the culmination of long years of exhaustive and thorough research. It is, in fact, the creation of "new knowledge".

The initiation of such invaluable work would not be possible were it not for the direct participation of world-famous research institutions and organisations.

Significantly, the goal at Ciba-Geigy echoes that of mankind's – freedom from suffering.

PAAB
CCPP

CIBA—GEIGY

Creating new knowledge for a healthier world.

When you get there, will the cupboard be bare?

Major new drugs don't just appear. It requires a substantial research commitment to discover, develope and evaluate them. The five leading prescription drugs today did not exist ten years ago. Ten years from now, many leading drugs will be replaced by newer, more effective medicines. Major advances in drug therapy have been a significant factor contributing to the standard of health care in Canada. Drug research means a lot to our continued good health. And that's why Merck Frosst is a leader in Canadian pharmaceutical research.

MF CANADA

MERCK FROSST CANADA INC.

KIRKLAND, QUÉBEC

Where today's research becomes tomorrow's therapy